Review Article

A Comprensive Review on Antiepileptic Medicinal Plants

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ABSTRACT

Epilepsy is the common neurological abnormality. It is a hyperexitation of neurones in the brain which leads to altered behaviour with/without violent motor activity. Various types of Seizures such as Partial seizures, Generalised seizures and Status epilepticus from these types Generalised seizures is more commonly seen in people. There are various types of factors which may lead to cause epilepsy like genetic or heredity, metabolic disorders, CNS infections, head injury etc. There are number of antiepileptic drugs are available in modern therapy but having chronic side effects. 1/3rd patients are resistant to antiepileptic drugs. In light to above the treatment of epilepsy with herbal drugs as adjuvant seems to be more beneficial and more effective to the patient with lesser side effects. Many research interpreted that the herbal medicines are used for epileptic condition to improve health. This review includes the botanical name, family, extract used along with doses and phytoconstituents of different reported antiepileptic medicinal plants. It also describes the model or method used for screening antiepileptic activity. Active constituents such as glycosides, alkaloids, flavonoids, saponins, proteins, tannins, steroids, fatty acids shows antiepileptic activity and in this review various plants reported these phytoconstituents. Further isolation of specific phytochemical constituent responsible for antiepileptic property is to be elucidated.

Keywords: Epilepsy, Seizures, Antiepileptics, Fabaceae.

INTRODUCTION

Epilepsy is the common neurological abnormality. It is a hyperexitation of neurones in the brain which leads to altered behaviour with/without violent motor activity. [1]Convulsion is the second most common neurologic disorder after stroke.[4] It is estimated that there are 55 lakhs people with epilepsy in India, 20 lakh in USA and 3 lakhs in UK. Each year about 1,25,000 new epilepsy cases occur out of these 30% are in people younger than age 18 at time of diagnosis.[2] Most of the epileptic patients need polytherapy of conventional antiepileptics and still not 100% cure. In antiepileptic drug therapy one third of patients remain unresponsive to the treatment. Cognitive impairment is major issue associated with long term use of antiepileptics. In addition to this oxidative stress has been implicated in the pathogenesis and progression of seizures. Major drawbacks due to currently available synthetic antiepileptic drugs are their chronic side effects and drug interactions which restricts their use.[4] Furthermore 30% of patients are refractory to the treatment of antiepileptics, which may need to develop novel drugs with varied mechanism of action having better efficacy and lesser side effects.[3]

TYPES OF SEIZURES[1,5]

Partial seizures

Neurological abnormality begins locally and often remains localised. These are further divided into

a) Simple partial seizures / Jacksonian seizure – It lasts for 20-60 seconds. It shows recurrent involuntary muscle contraction often limited to single limb or group of muscles like face, hand, and arm.

b) Complex partial seizures /Psychomotor seizures – This attack lasts for 2-5 minutes. Seizures generates from temporal lobe, and characterized by sudden onset of impaired consiousness and automatism i.e. purposeless movements, emotional changes, altered gait.

c) Secondary generalised seizures – The partial seizures occur first and then evolve into generalised tonic – clonic type of seizures. It is characterised by loss of consiousness with sustained contraction of muscle (tonic) which is followed by alternative contraction and relaxation.

Generalised seizures

It involves the neurological abnormal activity (excessive neuronal firing) throughout brain and which leads to immediate loss of consiousness.

a) Petitmal seizures/ Absence seizures - It is most common type of seizure. It is characterized by momentary loss of consiousness and intermittent jerking of hands may be observed.

b) Atonic seizures/ Akinetic seizures – It possesses symptoms like brief consiousness with relaxation of all muscles due to excessive inhibitory discharge

usually resulting in fall down with severe injury. This type of seizures mostly seen in children with diffuse encephalopathies.

c) Myoclonic – it is characterized by shock like contractions of muscle in extremities or over entire body; which results into falling down.

d) Grandmal seizures/ Tonic – clonic seizure – It begins with an abnormal electric discharge in small area of brain, which spreads all over adjoining parts quickly. This leads to temporal loss of consiousness with various symptoms like severe muscle spasm, jerky movements of body, intense turning of head to one side and loss of bladder control which causes frequent urination.

Status epilepticus

It is most serious form of epilepsy, defined as prolong seizure, either repetative seizure activity without full recovery of consiousness between the seizures, or continuous single seizure episode and it lasts for more than 30 min. It is a medical emergency.

Table 1: Etiology – Epilepsy possesses several causes which are presented below: [1, 5]

Genetic or heredity	Juvenile myoclonic epilepsy syndrome, childhood absence epilepsy syndrome, Juvenile absence epilepsy syndrome and progressive myoclonic epilepsy syndrome
Metabolic disorders	Alkalosis, Hypoparathyirodism, hypocalcemia, hyponitremia, hypoglycaemia, uremia, fever, phenyl, -ketonuria, vit B6 deficiency
CNS infections	Meningitis, encephalitis, neurosyphilis, toxoplasmosis, brain abscess
Cardiovascular disorders	Hypertensive encephalopathy
Cerebrovascular disorders	Hemorrhage , Thrombosis, cysts, hypoxia, stroke, aneurysms
Neurodegenerative disorders	Alzheimer's disease, multiple sclerosis
Head injury	Trauma, birth lesion, increased intracranial pressure.
Congenital disorders	Down's syndrome, Rubella infection (in utero)
Drug withdrawal	Alcohol, tranquilizers, sedatives and hypnotics
Drug and chemicals	Amphetamine, epinephrine, narcotics, excess insulin, lidocain, Pentylenetetrazole, lead, amytriptiline
Miscellaneous	Emotional stress, sleep deprivation, disco flashes, listening full blast Pop music (Musicogenic temporal lobe seizures)

Pathophysiology of Seizures

Seizures are the paroxymal manifestations of the cerebral cortex. Seizures occurs when the sudden imbalance between excitatory and inhibitory forces within the network of neurons.

Normally, neurons i.e. nerve cells communicates through membrane potential. An ion with positive and negative charges helps to create electric signals to be sent by the brain. When neuron is at resting membrane potential, then the negative charge inside the cell is more than the outside and vice versa.

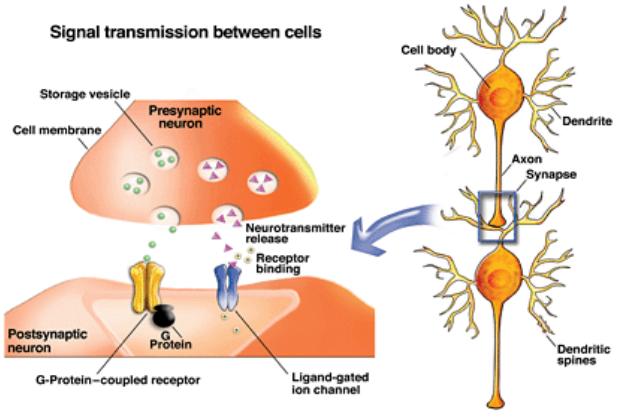

Figure 1: Signalling transmission in neruronal cell

During seizure episode, the membrane potential of neurons is altered in a way that causes hypersensitive or over activity of neurons due to certain stimuli/ triggering events.[1]

Neural basis of epilepsy

The reduction in inhibitory synaptic activity or enhanced excitatory synaptic activity which leads to cause seizures. The evolvement of neurotransmitters like GABA, Glycine (inhibitory) and Glutamate (excitatory) are predominantly involved.[6]

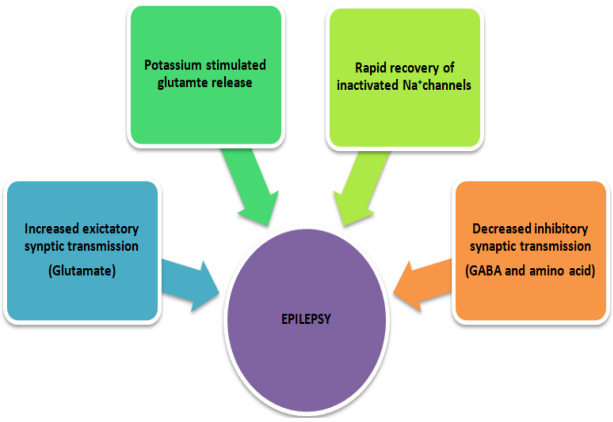

Figure 2: Neural Basis of Epilepsy

Table 2: List of medicinal plants showing antiepileptic activity.

Sr. No.	Name of plant (Family)	Extract and part used	Route and dose of extract	Experimental animal used	Screenig model used	Reference standard	Phytochemical constituents	References
1.	*Argyreia specicosa* (Convolvulaceae)	Hydroalcoholic extract of roots	100,200,400 mg/kg (p.o.)	Mice	PTZ MES	Clonazepam (0.1mg/kg, i.p.) Phenytoin (20mg/kg, i.p.)	Glycosides, alkaloids, amino acids, coumarin.	7
2.	*Allium cepha* (Liliaceae)	Hydroalcoholic extract of bulbs	100,200,400 mg/kg (p.o.)	Mice	PTZ MES	Diazepam (5 mg/kg, p.o.)	Carbohydrates, Amino acid, Alkaloids, glycosides,	8
3.	*Lycopersicon esculentum* (Solanaceae)	Petroleum ether and absolute ethanolic extract of fruits	50 mg/kg (p.o.)	Mice	MES	Phenytoin (25mg/kg, p.o.)	Glycosides, alkaloids, flavonoids, saponins, proteins, tannins, steroids, fatty acids.	9
4.	*Azima tetracantha* (Salvadoraceae)	Ethanolic extract of roots	250,500 mg/kg (i.p.)	Mice	MES PTZ	Sodium valproate (200mg/kg, i.p.)	Alkaloids, flavonoids and terpenoids	10
5.	*Brassica nigra* (Cruciferae)	Ethanolic extract of seeds	100,200 mg/kg (p.o.)	Rat	MES PTZ	Phenytoin (25mg/kg, i.p.) Diazepam (5mg/kg, i.p.)	Glycosides, flavonoids, alkaloids, carbohydrates, fixed oil and volatile oils.	11
6.	*Chrysanthellum indicum* Linn. (Compositae)	Methanollic extract of aerial parts of the plants	12.5, 25, 50 mg/kg (i.p.)	Mice	MES PTZ SIC	Phenytoin (20 mg/kg, i.p.)	Alkaloids, glycosides, tannins, saponins and flavonoids.	12
7.	*Ebenus stellata* (Fabaceae)	Ethanolic etract of aerial parts of the plant	2, 3, 5, 7 gm/kg	Mice	PTZ MES	Ethosuximide(150mg/kg, i.p.) Phenytoin (25mg/kg, i.p.)	Alkaloids,sterols, flavonoids, anthrone, anthroquinone, coumarin, tannins.	13
8.	*Erythriana mysorensis* (Fabaceae)	Chloroform extract of bark	200. 400 mg/kg (p.o.)	Rat	MES PTZ	Phenytoin (90 mg/kg, i.p.) Diazepam (4 mg/kg, i.p.)	Glycosides, alkaloids, flavonoids, tannins, terpenoids and saponins.	14
9.	*Glycine max* (Fabaceae)	Pet. ether and alcoholic extract of seeds	50mg/kg	Mice	MES	Phenytoin (25 mg/kg, p.o.)	Steroids, fatty acids, saponins, flavonoids, glycosides, carbohydrates, Tannins ,proteins.	15
10.	*Leucas martinicensis* (Lamiaceae)	Aqueous extract of leaves	50, 100, 200, 400 mg/kg (i.p.)	Rat	MES Strychnine induced convulsions	Diazepam (3mg/kg, i.p.)	Alkaloids, saponins, flavonoids, glycosides	16
11.	*Moringa Oleifera* (Moringaceae)	Ethanolic extract of leaves	200 mg/kg (p.o.)	Mice	MES PTZ	Phenytoin (25 mg/kg, i.p.) Sodium valproate (75 mg/kg ,i.p.)	Alkaloids, flavonoids, anthocyanin, proanthocyanin, cinnamates.	17
12.	*Mucuna prurience* (Fabaceae)	Butanolic extract of seed	100, 200 mg/kg (p.o.)	Mice	PTZ MES	Sodium valproate (50 mg/kg, i.p.) Diphenylhydantoin (20mg/kg, i.p.)	Tannins, saponins, alkaloids, flavonoids, cynogenic glycosides, oxalate, phytate.	18
13.	*Nigella sativa* (Ranuculaceae)	Aqueous extract of seeds	200, 400, 600 mg/kg (p.o.)	Rat	PTZ	Sodium valproate (300mg/kg, i.p.)	Flavonoids, anthocyanins, alkaloids, essential fatty acids	19

							like linoleic acid, oleic acid,	
14.	*Ocimum basillum* (Liliaceae)	Hydroalcoholic extract of leaves	100, 20, 300, 350 mg/kg (i.p.)	Mice	PTZ	Diazepam (2 mg/kg, i.p.)	1-8 cineole, linalool, gerniol, 93% essential oils	20
15.	*Phyllostachys bambusoides* (Phocaea)	Chloroform extract of leaves	200 mg/kg (p.o.)	Rat	MES	Diazepam (4mg/kg, i.p.)	Carbohydrates, alkaloids, tannins, flavonoids, proteins, saponins, glycosides.	21
16.	*Pistacia vera* (Portulacae)	Ethanolic extract of fruits	50, 100 mg/kg (p.o.)	Rat	Kindling model	Diazepam (1 mg/kg, i.p.)	Phenolic compounds, terpenoids, monoterpens, flavonoids, alkaloids, saponins, fatty acids, sterols.	22
17.	Portulaca oleracea (Portulacacae)	Aqueos extract of leaves	200, 400, 600 mg/kg (p.o.)	Mice	MES PTZ	Phenytoin (20 mg/kg, p.o.) Sodium valproate (200 mg/kg, p.o.)	Flavonoids, alkaloids, omega – 3 fatty acids, antioxidant.	23
18.	*Spinacia Oleracea* (Amaranthaceae)	Aqueous extract of leaves	400 mg/kg (p.o.)	Rat	Amygdala kindling model	Diazepam (20 mg/kg, i.p.)	Vitamin – C, E,A, Folic acid, calcium, magnesium, manganese.	24
19.	*Tricosanthes dioica* (Cucurbitaceae)	Aqueous extract of fruits	400 mg/kg (p.o.)	Mice	MES PTZ	Phenytoin (25 mg/kg, i.p.)	Saponins, glycosides,alkaloids	25
20.	*Trigonella foeum – gracum* (Fabaceae)	Methanollic extract of seeds	50, 100, 200 mg/kg (p.o.)	Rat	Strychnine	Diazepam (1 mg/kg, p.o.)	Saponin, alkaloids, amino acid and flavonoids.	26
21.	*Vigna radiata* (Fabaceae)	Methanolic and chloroform extract of leaves	100, 250 mg/kg (p.o.)	Rat	MES	Phenytoin (25mg/kg, i. p.)	Energy, carbohydrates, fats, protein, vitamins, minerals.	27
22.	*Zingiber officinale* (Zingiberaceae)	Ethanolic extract of rhizomes	100, 200 mg/kg (p.o.)	Mice	MES	Phenytoin (25 mg/kg, i.p.)	Gingerols, shagols, paradols, zingerone, phytosterols, diarylheptanoids.	28
23.	*Anethum graveolens* (Apiaceae)	Aqueous extract of leaves	100, 250, 400 mg/kg (p.o.)	Mice	PTZ kindling model	Sodium valproate (100 mg/kg, i.p.)	Flavonoids, coumarins, phenolic acids, steroids.	29
24.	*Cassia auriculata* (Caesalpiaceae)	Pet. ether, chloroform, ethanolic and aqueous extract of leaves	250, 500 mg/kg (p.o.)	Rat	MES PTZ	Phenytoin (25mg/kg, p.o.) Diazepam (4mg/kg, p.o.)	Carbohydrates, proteins, amino acids, lipids, glycosides, flavanols, flavonoids, tannins and phenolic compounds.	30
25.	Canna indica (Cannaceae)	Methanolic extract of aerials parts of plant	100, 200, 400 mg/kg (p.o.)	Mice	MES Isoniazid induced convulsions Strychnine induced convulsion	Phenytoin (50 mg/kg, i.p.) Diazepam (1mg/kg, i.p.)	Alkaloids, carbohydrates, flavonoids, proteins, amino acids, steroids, fat and oils, saponins, phenols, starch.	31

CONCLUSION

Epilepsy is one of the most common neurological disorders. All antiepileptics available in market having some ADR, this leads to neuronal cell loss and neurodegeneration. Therefore there is need to search safe and effective drug for epilepsy. As a result of this researchers are focusing on the therapeutic effects of medicinal plants having antiepileptic activity. Further isolation of active phytoconstituents helps to improve health benefits.

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