Pharmacognosy Reviews [Phcog Rev.]
Vol 2, Issue 4, Jul-Dec, 2008
Page 229-240

PHCOG REV.
An official Publication of Phcog.Net

PHCOG REV.: Review Article

Advancements in Traditional Medicinal Plants Used in Epilepsy

Shubhini A. Saraf, Rajiv Gupta, Anurag Mishra, Ashish Kumar Sharma and Rajesh Kumar Punia*

Faculty of Pharmacy, Babu Banarasi Das National Institute of Technology & Management (BBDNIT&M), Sector I, Dr. Akhilesh Das Nagar, Faizabad Road, Lucknow, U.P., India
**For Correspondence: rpunia2003@yahoo.com*

ABSTRACT

From the times immemorial plants have been used by mankind for their relieving and therapeutic abilities and still we rely on their healing properties. Plants having active constituent have a direct pharmacological action on our body including various organs. One such major organ is brain, so complex that still only few drugs are approved by drug authorities for ailments like epilepsy. The Indian system of medicine "Ayurveda" classified the plants affecting our brain. Epilepsy is one such condition and may be defined as a neuropsychological disorder, which occurs due to over discharge of neurotransmitter substance. Epilepsy differs from seizure; a seizure is the paroxysmal events due to abnormal excessive hyper synchronous discharge from an aggregate of central nervous system (CNS) neurons. Epilepsy describes a condition in which a person has recurrent seizures, due to chronic underlying process. There are number of drugs available for treatment of epilepsy in modern therapy. But the major disadvantage being faced is their chronic side effects. Treatment of epilepsy with herbal drugs as adjuvant seems to be more beneficial and is gaining more popularity due to their fewer side effects. Herbal drugs are acting at target site having same mechanism of action as that of synthetic drugs. There are number of drugs being used in the traditional medicine for treatment of epilepsy and presently many of these drugs are being explored scientifically to ascertain their anticonvulsant activity. This review compiles the work done regarding the newly explored medicinal plants for anticonvulsant activity along with their mechanism of action.

Key Words :

INTRODUCTION

Epilepsy is a condition in which a person has recurrent seizures. A seizure is defined as an abnormal, disorderly discharging of the brain's nerve cells, resulting in a temporary disturbance of motor, sensory, or mental function. There are many types of seizures, depending primarily on which part of the brain is involved. The term epilepsy says nothing about the type of seizure or cause of the seizure, only that the seizures happen again and again. A stricter definition of the term requires that the seizures have no known underlying cause. This may also be called primary or idiopathic epilepsy. Episodes of abnormal electrical activity within the brain result in seizures. The specific area of the brain affected by the abnormal electrical activity may result in a particular type of seizure. If all areas of the brain are affected by the abnormal electrical activity, a generalized seizure may result. This means that consciousness is lost or impaired. Often all the person's arms and legs stiffen and then jerk rhythmically. One seizure type may evolve into another during the course of the seizure. For example, a seizure may start as a partial, or focal, seizure, involving the face or arm. Then the muscular activity spreads to other areas of the body. In this way, the seizure becomes generalized. Seizures caused by high fevers in children are not considered epilepsy.

Causes of Epilepsy

Healthy people may have seizures under certain circumstances. If the seizures have a known cause, the condition is referred to as secondary or symptomatic epilepsy. Some of the more common causes include the following: Tumor, Chemical imbalance such as low blood sugar or sodium, Head injuries, Certain toxic chemicals or drugs of abuse, Alcohol withdrawal, Stroke including hemorrhage, Birth injuries.

EPILEPSY CLASSIFICATION:

Generalized seizures:

1. Generalized tonic-clonic seizures or Grand mal
2. Absence seizure or petit mal
3. Atonic seizure
4. Myoclonic seizure

Partial or focal seizures:

1. Simple partial seizure
2. Complex partial seizure
3. Simple partial seizure or Complex partial seizure secondarily generalized

Modern Antiepileptic Therapy And Their Adverse Effects

Classification on the basis of mechanism of action

1. Prolongation of Sodium channel inactivation: Phenytoin, Carbamazepine, Valproate, Lamotrigine.
2. Facilitation of GABA mediated Chlorine ion cannel opening: Barbiturates, Benzodiazepine, Vigabatrin, Valproate, Gapapentin.
3. Inhibition of 'T' type Calcium current: Ethosuximide, Trimethadione, Valproate.

Adverse effects: Sedation, dizziness, vertigo, diplopia, atxia, vomiting, diarrhea and anorexia. Acute intoxication causes coma, convulsion and cardiovascular collapse. Hypersensitivity reactions are rashes, photosensitivity, hepatitis, lupus like syndrome. Some degree of leucopenia

due to hypersensitivity is more common. They are also teratogenic in nature (1). Due to the intense side effect of modern drug treatment, the herbal treatment is gaining more popularity. They are safe in use as compared to conventional drug treatment.

HERBAL THERAPY

Taxus wallichiana

Taxus wallichiana Zucc. (Himalayan Yew) is often used in northern areas of Pakistan for the treatment of pyrexia, acute pains and epilepsy. A search was carried out to ascertain pharmacological activities of the methanol leaf extract against convulsion, nociception and pyrexia induced in rodents. The studies were carried out using acetic acid-induced nociception and pentylenetetrazole-induced convulsions in mice, while formalin tests and yeast-induced pyrexia in rats. Significant analgesic (67.77 and 74.29%) effect was found in acetic acid-induced model at doses of 100 and 200 mg/kg, i.p. respectively. Crude extract exhibited significant ($P < 0.05$) inhibition of the formalin noxious stimulation on both early and late phases of pain by the extracts (100 and 200 mg/kg doses). Plant extract has controlled the pentylenetetrazole-induced convulsions in mice. 100 and 200 mg/kg i.p doses of the extract significantly ($P < 0.05$) inhibited the mioclonus and clonus while inhibition of tonus and hind limb tonic extension (HLTE) was highly significant ($P < 0.01$). The anticonvulsant activity of this plant has been reported for the first time throughout the whole genus. The observed pharmacological activities provide the scientific basis for the folkloric use of the plant in treating epilepsy, pyrexia and acute pain (2).

Nardostachys jatamansi

Ethanol extract of the roots of *Nardostachys jatamansi* DC. (Valerianaceae) was studied for its anticonvulsant activity and neurotoxicity, alone and in combination with phenytoin in rats. The results demonstrated a significant increase in the seizure threshold by *Nardostachys jatamansi* root extract against maximal electroshock seizure (MES) model as indicated by a decrease in the extension/flexion (E/F) ratio. However, the extract was ineffective against pentylenetetrazole induced seizures. *Nardostachys jatamansi* root extract also showed minimal neurotoxicity against rotarod test at doses that increased the seizure threshold. Further, pretreatment of rats with phenytoin at a dose of 12.5, 25, 50 and 75 mg/kg in combination with 50 mg/kg of *Nardostachys jatamansi* root extract resulted in a significant increase in the protective index (PI) of phenytoin from 3.63 to 13.18. The dose response studies of phenytoin alone and in combination with *Nardostachys jatamansi* extract on the serum levels of phenytoin clearly demonstrated the synergistic action of both the drugs (3).

Scutellaria baicalensis

Sedative effects of *Scutellaria baicalensis* extracts and found that these extracts or their constituents may also have anticonvulsive effect. Wogonin is a natural product isolated from *S. baicalensis*, which possesses central nervous system effects such as anxiolytic and neuroprotective activities. A study was carried out to investigate the effects of wogonin on convulsion related behaviors, such as myorelaxation, motor coordination, and anticonvulsant effects of wogonin on chemical induced seizure and electroshock seizure in mice or rats. Wogonin injected intraperitoneally significantly blocked convulsion induced by pentylenetetrazole and electroshock but not convulsion induced by strychnine. Wogonin also significantly reduced the electrogenic response score, but flumazenil treatment reversed this decrease to the level of the control group. The wogonin increased Cl^-influx whereas Flumazenil and bicuculline inhibit it. These results indicate that the anticonvulsive effects produced by wogonin were mediated by the GABAergic neuron (4).

Flavonoids

Various synthetic derivatives of natural flavonoids are known to have neuroactive properties. A search was carried out to investigate the anticonvulsant effects of rutin (3, 3′, 4′, 5, 7-pentahydrohyflavone-3-rhamnoglucoside), a flavonoid which is an important dietary constituent of food and plant-based beverages. To this end, we assessed the anticonvulsant effects of rutin in rats treated with pentylenetetrazole (PTZ) (90 mg/kg, i.p.) and sought to clarify this mechanism. Intracerebroventricular (i.c.v.) injection of rutin dose-dependently affected minimal clonic seizures (MCS) and generalized tonic–clonic seizures (GTCS) induced by PTZ, through increments in seizure onset. Additionally, pretreatment with flumazenil (5 nM, i.c.v.) abolished the anticonvulsant effects of rutin during the onset of both seizures. These results indicated that rutin has anticonvulsant effects in the brain, possibly through positive allosteric modulation of the $GABA_A$ receptor complex via interaction at the benzodiazepine site (5).

Cestrum nocturnum

Cestrum nocturnum is a garden shrub from the family *Solanaceae* and is used as a remedy for different health disorders. Decoctions obtained from dried leaves of the plant were tested in different neuropharmacological models (Irwin test, exploratory behavior, tests for analgesia, isoniazid- and picrotoxin-induced convulsions, and maximal electroshock seizures) in mice, as well as in amphetamine-induced stereotypies and penicillin epileptic foci in rats. Decoctions from dried leaves induced restlessness, passivity and significantly reduced exploratory behavior and amphetamine-induced stereotypies. The decoctions were not effective against pharmacologically induced convulsions. However, repeated administration of five doses at 1-hour intervals reduced the amplitude of penicillin-induced epileptic spikes in both primary and secondary foci, in curarized rats (6).

Bacopa monnieri

The potential for antiepileptic drugs to negatively impact cognitive abilities has generated renewed interest in herbal drugs and formulations in the treatment of epilepsy. *Bacopa monnieri* is one such widely used revitalizing herb that purportedly strengthens nervous function and also possesses memory-enhancing, antioxidative, antiepileptic and anti-inflammatory properties. The neuroprotective role of *B. monnieri* extract in alteration of glutamate receptor binding and gene expression of NMDA R1 in hippocampus of temporal lobe epileptic rats were observed. In association with pilocarpine-induced epilepsy, there was significant down

PHCOG REV.
An official Publication of Phcog.Net

Table 1: List of Southern African Plants for Epilepsy

Family	Species	Part used	Extraction solvent
Amaryllidaceae	*Brunsvigia grandiflora*	Leave	Water
Anacardiaceae	*Rhus chirindensis*	Leave, Root	Water, Ethanol
	Rhus rehmanniana	Leave	Water, Ethanol
Apocynaceae	*Acokanthera oblongifolia*	Leave	Water, Ethanol
Araliaceae	*Cussonia sp.*	Leave	Water, Ethanol
	Cussonia spicata	Root	Water, Ethanol
Asphodelacea	*Bulbine frutescens*	Root, stem	Water, Ethanol
	Gasteria croucheh	Leave	Water, Ethanol
Combretaceae	*Combreturn bracteosum*	Root	Water, Ethanol
Euphorbiaceae	*Antedesma venonum*	Leave	Water, Ethanol
	Hypoxis colchicifolia,	Corm	Ethanol
	Hoslundia opposita	Corm	Ethanol

Table 2: Plants Used in the Treatment of Epilepsy by Traditional Healers in Dar Es Salaam, Tanzania

Botanical name	**Part used**	**Method of preparation**	**Route and method of administration**
Abrus precatorius L. (Leguminosae)	Leaves	The leaves are boiled with water	Oral; three table spoonfuls are taken twice daily
Abrus schimperiana Hochst. ex Benth. (Leguminosae)	Leaves	Used to make a tea	Oral; half a cup of tea is taken three times a day
Acacia glaucophylla Steud. ex A. Rich. (Leguminosae)	Leaves	Leaves are burnt	Inhalation; the patient is covered with a blanket and made to inhale the smoke
Acalypha ornata Hochst. ex A. Rich. (Euphorbiaceae)	Stem barks	Stem is burnt on broken pot	Inhalation: smoke is inhaled twice a day
Adhatoda engleriana Lindau (Acanthaceae)	Roots	The roots are powdered	Oral; three table spoonfuls are mixed with water and chewed three times a day
Afzelia quanzensis Welw. (Leguminosae)	Roots	Powdered and soaked in water	Topical; soaked powder is applied topically by rubbing the forehead
Ageratum conyzoides L. (Compositae)	Seeds	Boiled with water	Oral; three table spoonfuls given three times a day
Albizzia bradycalyx Oliv. (Leguminosae)	Stem barks	Boiled with water	Oral; quarter a cup taken three times a day
Albizia anthelmintica A. Brongn. (Leguminosae)	Leaves, roots	Leaves boiled with water	Oral; one cup is taken three times a day
		Roots boiled with water	
Aloe sp. (Liliaceae)	Roots	Boiled with water	Oral; one table spoonful is taken three times a day
Antidesma venosum E. Mey. (Euphorbiaceae)	Roots	Roots boiled with water	Oral; three teaspoons taken twice a day
Apodytes dimidiata E. Mey. ex Benth. (Icacinaceae)	Leaves, stem barks	Leaves boiled with water	Oral; one tea cup of decoction taken orally, twice a day
Aristolochia parensis Engl. (Aristolochiaceae)	Roots	Boiled with water	Oral; one table spoonful taken twice a day

Botanical name	Part used	Method of preparation	Route and method of administration
Boscia kirkii Oliv. (Capparidaceae)	Roots	Boiled with water	Oral; half a cup taken twice a day
Canthium hispidum Benth. (Rubiaceae)	Roots	Boiled with chicken fat and water	Oral; quarter a cup is taken twice a day
Cassia fistula L. (Leguminosae)	Leaves	Rolled and mixed with milk	Oral; chewed with the milk two times a day
Chrysanthemoides monilifera (L.) J. Mort. ssp. *septentrionalis* T. Norton (Compositae)	Stem barks	Boiled with water	Oral; one cup is taken twice a day
Cissus quadrangularis L. (Vitaceae)	Leaves	Boil with water	Oral; two table spoonfuls taken three times a day
Clausena anisata (Willd.) Hook. f. ex Benth. (Rutaceae)	Roots, leaves	Boil with water	Inhalation; patient is covered with a blanket and made to inhale the steam
Commiphora pilosa Engl. (Burseraceae)	Stem bark, roots	Boiled with water	Oral; three table spoonfuls twice a day
Curcuma longa L. (Zingiberaceae)	Leaves	Boiled with water	Oral; one cup taken three times a day
			Inhalation; steam is inhaled once a day
Cussonia spicata Thunb. (Araliaceae)	Leaves	Boiled with water	Oral; two table spoonfuls three times a day
Cussonia zimmermannii Harns (Araliaceae)	Roots	Powdered roots	Oral; one tea spoon taken with water three times a day
Cynotis nudiflora Kunth (Compositae)	Stem barks, roots	Boiled with water	Oral; one tea cup taken three times a day
Dioscorea preussii Pax (Dioscoreaceae)	Roots	Boiled with water	Oral; one cup taken three times a day
Dodonaea schiedeana Schltr. (Sapindaceae)	Roots	Boiled with water	Oral; half a cup taken three times a day
Ehretia amoena Klotzsch (Boraginaceae)	Roots	Boiled with chicken	Oral; one cup taken twice a day
Elaeodendron stuhlmannii Loes. (Celastraceae)	Stem barks	Boiled with water	Oral; quarter a cup taken twice a day
Encephalartos hildebrandtii A. Br. & Bouché (Zamiaceae)	Stem barks	Not revealed	Not revealed
Erythrophleum guineense G. Don. (Leguminosae)	Roots	Boiled with water	Oral; quarter a cup taken three times a day
Euclea fructuosa Hiern. (Ebenaceae)	Leaves	Powdered leaves boiled with water	Inhalation; steam inhaled twice a day
Fernandoa magnifica Seem. (Bignoniaceae)	Roots	Roots are powdered	Oral; three table spoonfuls are taken with tea twice a day
Ficus schimperiana Hochst. ex Miq. (Moraceae)	Stem barks	Boiled with water	Oral; three table spoonfuls taken twice a day
Ficus sycomorus L. (Moraceae)	Barks	Boiled with water	Oral; quarter of a cup three times a day
Grewia bicolor Juss. (Tiliaceae)	Leaves	Boiled with water	Oral; half a tea cup taken three times a day
Harrisonia abyssinica Oliv. (Simaroubaceae)	Roots	Boiled with water	Oral; two table spoonfuls taken twice a day
Heeria insignis (Del.) O. Ktze. (Anacardiaceae)	Roots	Boiled with water	Oral; one cup taken three times a day
*Hibiscus subdariffa*L. (Malvaceae)	leaves	Crushed leaves are soaked with water for 12 h	Oral; one cup of tea is taken three times a day

Botanical name	Part used	Method of preparation	Route and method of administration
Hoslundia opposita Vahl. (Labiatae)	Roots, stem barks	Boiled with water	Oral; three table spoonfuls taken twice a day
Lobelia anceps L.f. (Campanulaceae)	Leaves	Boiled with water	Half a cup taken once a day
Lonchocarpus capassa Rolfe (Leguminosae)	Roots	Boiled and burnt	Inhalation; patient is covered with a bed sheet and made to inhale the smoke
Maerua cylindricarpa Gilg and Ben. (Capparidaceae)	Leaves	Not revealed	Not revealed
Myrica kilimandscharica Engl. (Myricaceae)	Roots	Boiled with water	Oral; quarter of a cup taken three times a day
Ocimum suave Willd. (Labiatae)	Leaves	Leaves are crushed	Topical; used to rub the forehead twice a day
Oplismenus hirtellus (L.) P. Beauv. (Gramineae)	leaves	Boiled with water and filtered	Oral; half a cup of tea taken twice a day
Pouzolzia hypoleuca Wedd. (Urticaceae)	Roots	Not revealed	Not revealed
Randia kraussii Harv. ev. Msonju (Rubiaceae)	Roots	Boiled with water	Oral; half a cup of tea taken twice a day
Rauvolfia rosea K. Schum. (Apocynaceae)	Roots	Powdered roots soaked over night with a local brew	Oral; one table spoonful taken twice a day
Rottboellia exaltata L.f. (Gramineae)	Roots	Powder is mixed with cooking oil and left for 2 days	Topical; the patient is made to shave the head and rub it with the mixture once or twice a day
Salacia stuhlmanniana Loes. (Celestraceae)	Stem barks	Powdered stem is boiled with water	Oral; two tablespoonfuls taken orally three times a day
Schlechterina mitostemmatoides Harms (Passifloracae)	Stem barks	Not revealed	Not revealed
Tamarindus indica L. (Leguminosae)	Roots	Boil the roots with water	Oral; one cup of the decoction taken twice a day
Teclea nobilis Delile (Rutaceae)	Roots	Boiled with water	Oral; half a cup taken twice a day
Tephrosia aequilata Bak. (Leguminosae)	Stem barks	Fresh barks are crush and then boiled with water	Oral; one table spoonful taken three times a day
Uvaria leptocladon Oliv. (Annonaceae)	Stem bark	Not revealed	Not revealed
Vitex mombassae Vatke. (Verbenaceae)	Roots	Roots are ground into a powder	Oral; one table spoon is taken with porridge three times a day
Waburgia stuhlmannii Engl. (Capparidaceae)	Stem barks	Boiled with water	Oral; two cups are taken twice a day
Warburgia ugandensis Sprague. (Canellaceae)	Stem bark	Scraped into a fine powder	Oral; one cup taken with tea twice a day
Xylopia arenaria Engl. (Annonaceae)	Roots		
Zanthoxylum chalybeum Engl. (Rutaceae)	Roots	Boiled with water	Oral; three spoonfuls taken three times a day

regulation of NMDA R1 gene expression and glutamate receptor binding without any change in its affinity. *B. monnieri* treatment of epileptic rats significantly reversed the expression of NMDA R1 and glutamate receptor binding alterations to near-control levels. Also, in the epileptic rats, it was observed a significant increase in the activity of glutamate dehydrogenase, which neared the control level after *B. monnieri* treatment. The therapeutic effect of *B. monnieri* was also observed in the Morris water maze experiment. These data together indicate the neuroprotective role of *B. monnieri* extract in glutamate-mediated excitotoxicity during seizures and cognitive damage occurring in association with pilocarpine-induced epilepsy (7).

Traditional Chinese herbal medicine

Traditional Chinese herbal medicine is the most widely practiced form of herbalism worldwide. Most traditional therapeutic formulations consist of a combination of several drugs. The combination of multiple drugs is thought to maximize therapeutic efficacy by facilitating synergistic actions and ameliorating or preventing potential adverse effects while at the same time aiming at multiple targets. A research program was initiated to characterize *in vitro* molecular actions of a collection of 58 traditional Chinese drugs that are often used for the treatment of stroke. The results indicate that these drugs possess activity at disparate molecular targets in the signaling pathways involved in *N*-methyl-d-aspartate (NMDA) receptor-mediated neuronal injury and death. Each herbal drug contains diverse families of chemical compounds, where each family comprises structurally related members that act with low affinity at multiple molecular targets. The data appear to support the multicomponent, multitarget approach of traditional Chinese medicine. Glutamate release and excessive stimulation of NMDA receptors cause status epilepticus-induced neuronal death and are involved in epileptogenesis. Therefore, these results are also relevant to the development of antiepileptogenic and neuroprotective therapy for seizures. The combination of principles of modern molecular medicine with certain ideas of traditional empirical Chinese medicine may be beneficial in translational medicine in general. Formulation of *Tianma Gouteng Yin Concha Haliotidis* (1), *Ramulus uncariae* cum uncis (2), *Herba Taxilli* (3), *Caulis Polygoni* multiflori (4), *Radix scutellariae* (5), *Radix achyranthis* bidentatae (6), *Fructus gardeniae* (7), *Rhizoma gastrodiae* (8), *Poria cum ligno* hospite (9), *Cortex eucommiae* (10), and *Herba leonuri* (11). Examples of the structural variety of chemical compounds isolated from the ingredients of *Tianma gouteng Yin*. Chrysophanol is an anthraquinone from *Polygonum multiflorum*. Stigmasterol is a phytosterol from *Gardenia jasmonides*. Betulin is a triterpenoid from *Eucommia ulmoides*. Baicalin is a flavonoid from *Scutellaria baicalensis*. Rhynchophylline is an alkaloid from *Uncaria rhynchophylla*. Vanillin is a phenolic compound from *Gastrodia elata*. Chitin is a polyglucan from *Concha haliotidis*. Palmitic acid is a fatty acid from *Poria cocos* (8).

Spondias mombin

In a study the effects of air-dried *Spondias mombin* leaves extracted with aqueous, methanol and ethanol solvents on hexobarbital-induced sleeping time and novelty-induced rearing (NIR) behaviours in mice and rats were evaluated. The effect of the extracts on amphetamine- and apomorphine-induced stereotyped and picrotoxin-induced convulsive behaviour in rats were also observed. The methanolic and ethanolic extracts prolonged the hexobarbital-induced sleeping time and reduced the NIR in both mice and rat in a dose-dependent manner. The aqueous extract prolonged the hexobarbital-induced sleeping time and reduced novelty-induced rearing (NIR). The inhibitory effect of the extracts on NIR was not reversed by atropine, yohimbine, naltrexone and flumazenil. However, the extracts blocked the facilitating effect of flumazenil. This suggests that NIR inhibitory effects of extracts of *Spondia mombin* are not mediated via muscarinic, α_2 adrenergic, and μ-opioid receptors, whereas, the extracts appear to facilitate GABAergic transmission. In addition the extracts blocked picrotoxin-induced convulsions. Phenolic compound(s) were present in the ethanolic and methanolic extracts, which exhibited anticonvulsant properties in the picrotoxin-induced convulsions model. The extracts decreases the amphetamine/apomorphine-induced stereotyped behaviour, which suggested that these extracts possess antidopaminergic activity. The effect of the extracts on hexobarbitone-induced sleeping time was blocked by flumazenil a $GABA_A$ antagonist, indicating that the extracts contain $GABA_A$ agonists. These results suggested that the leaves extracts of *Spondias mombin* possess sedative and antidopaminergic effects (9).

Sanseviera liberica

The central nervous system (CNS) depressant and anticonvulsant activities of the aqueous root extract of *Sanseviera liberica* were investigated on various animal models including pentobarbitone sleeping time and hole-board exploratory behaviour for sedation tests, and strychnine, picrotoxin, bicuculline and pentylenetetrazole-induced convulsions in mice. Aqueous root extract, like chlorpromazine HCl produced a dose-dependent prolongation of pentobarbitone sleeping time and suppression of exploratory behavior. Aqueous extract at a dose 100mg/kg and 200 mg/kg produced dose-dependent and significant ($P < 0.05$) increases in onset to clonic and tonic convulsions, and at 400 mg/kg, showed complete protection against seizures induced by strychnine, picrotoxin and bicuculline, but not with pentylenetetrazole. Preliminary phytochemical investigations of aqueous root extract revealed the presence of carbohydrates, alkaloids, saponins, reducing sugars and oils. The results indicate that the aqueous root extract has sedative and anticonvulsant activities, therefore, justified its use in traditional African medicine (10).

Withania somnifera

In an experimental model, i.e. status epilepticus, *Withania somnifera* was given acutely and it delayed the onset of forelimb clonus and rearing but the drug was not able to reduce the mortality rate against lithium-pilocarpine-induced status epilepticus in rats. When the root extract of *W. somnifera* was given chronically for 7 days followed by lithium-pilocarpine challenge, it protected the animal from mortality up to 60% but did not reduce the latency of forelimb clonus with rearing. Furthermore, *W. somnifera* was also combined with the standard antiepileptic drugs. When *W. somnifera* was combined with these standards agents, the combination was able to reduce significantly the effective dose of diazepam and clonazepam to offer full protection with no mortality

Molecular studies

The profound anticonvulsant activity of *W. somnifera* root extract as reported in various animal models is hypothesized to be through $GABA_A$ receptors. The $GABA_A$-benzodiazepine receptor-ionophore complex is a major site of drug action for a variety of centrally acting drugs including benzodiazepines and barbiturates and Barbiturates and benzodiazepines

facilitate the effect of GABA mediated Cl^- conductance. *W. somnifera* root extract is reported to have anxiolytic and CNS inhibitory effects. An experiment was conducted to determine the modulatory effect of a methanol extract of *W. somnifera* on the binding of [^{3}H] GABA, [^{35}S] *t*-butylbicyclophosphorothionate (TBPS) and [^{3}H] flunitrazepam to their respective sites in brain neurons. The methanol extract of *W. somnifera* produced a concentration-dependent inhibition of both [^{3}H] GABA and [^{35}S] TBPS binding in rat cerebral cortical membranes. The extract was more potent in inhibiting [^{3}H] GABA and [^{35}S] TBPS binding. The methanol extract of *W. somnifera* increased the specific binding of [^{3}H] flunitrazepam in cerebral cortex. Also the effect of extract on [^{3}H] flunitrazepam binding was additive with that of pentobarbital. When the extract and GABA were tested in combination on [^{3}H] flunitrazepam binding the effect was not additive. The effect of combination treatment indicated that the extract decreased the enhancing effect of GABA. Similar results were obtained when the effect of two GABA agonists (GABA and muscimol) was examined in [^{3}H] flunitrazepam binding. These functional studies indicated that *W. somnifera* possessed its anticonvulsant activities through $GABA_A$ receptor system (11).

Vitex agnus

The antiepileptic activity of hydrophilic extract of *Vitex agnus castus* fruit (*Vitex*) was evaluated by the kindling model of epilepsy. Intact male rats were stereotaxically implanted with a tripolar and two monopolar electrodes in amygdala and dura, respectively. The after discharge threshold was determined in each animal and stimulated daily until fully kindled. This data showed that even low dose (60 mg/kg) of *Vitex* could significantly increase the after discharge threshold and decrease the after discharge duration and stage 5 duration ($P < 0.05$). These changes were more significant with higher doses (120 or 180 mg/kg) for after discharge duration ($P < 0.01$) and stage 5 duration ($P < 0.001$). *Vitex* at the dose of 120 mg/kg induced significant increment in S4L ($P < 0.05$). This effect was more prominent at the dose of 180 mg/kg ($P < 0.001$). The latter dose could significantly reduce seizure stage ($P < 0.01$) and most of the animals did not show stage 5. These results indicate that *Vitex* can reduce or prevent epileptic activity as demonstrated by reduction of after discharge duration and stage 5 duration (length of convulsion) in a dose dependent manner. In conclusion, *Vitex* at appropriate dose can probably reduce or control epileptic activities (12).

Leonotis leonurus

Water extract of *Leonotis leonurus* was tested for anticonvulsant activity against seizures produced in mice by pentylenetetrazole, picrotoxin, bicuculline and N-methyl-DL-aspartic acid (intraperitoneal injections). *L. leonurus* extract in the doses of 200 and 400 mg/kg respectively protected 37.5% and 50% of animals used and significantly ($p < 0.05$) delayed pentylenetetrazole (90 mg/kg)-induced tonic seizures. Similarly, the same doses of *L. leonurus* extract significantly ($p < 0.05$) delayed the onset of tonic seizures produced by picrotoxin (8 mg/kg) and N-methyl-DL-aspartic acid (400 mg/kg). However, all the doses of aqueous extract of *L leonurus* used did not alter the seizures induced by bicuculline (20 mg/kg) to any significant extent. The data suggested that the extract of *L. leonurus* has anticonvulsant activity and may probably be acting through non-specific mechanisms, since it affects both gabaergic and glutaminergic systems. High performance liquid chromatography (HPLC) and phytochemical tests carried out respectively show a spectrum profile, characteristic of *L. leonurus* and the presence of alkaloids, saponins and tannins in the extract (13).

Cotyledon orbiculata

The anticonvulsant activity of *Cotyledon orbiculata* L. (Crassulaceae) was investigated by studying the effects of both aqueous and methanol extracts of the plant species on seizures induced by pentylenetetrazole, bicuculline, picrotoxin and *N*-methyl-dl-aspartic in mice. Aqueous extract of *Cotyledon orbiculata* (50–400 mg/kg, i.p.) and methanol extract (100–400 mg/kg, i.p.) significantly prolonged the onset of tonic seizures induced by pentylenetetrazole. Methanol extract (400 mg/kg, i.p.) also significantly reduced the incidence of the seizures. One hundred to two hundred milligrams/kilogram (i.p.) of aqueous extract of *Cotyledon orbiculata* significantly delayed the onset of the tonic seizures induced by bicuculline, picrotoxin and *N*-methyl-dl-aspartic acid. Similarly, methanol extract (100–400 mg/kg, i.p.) significantly delayed the onset of the tonic seizures induced by bicuculline and picrotoxin while 100 mg/kg (i.p.) significantly delayed the onset of *N*-methyl-dl-aspartic acid induced seizures. Methanol extract (200 mg/kg, i.p.) significantly reduced the incidence of the seizures induced by bicuculline. The obtained data suggest that both aqueous and methanol extracts of *Cotyledon orbiculata* have anticonvulsant property and may probably be affecting both gabaergic and glutaminergic mechanisms to exert its effect. The phytochemical analysis revealed the presence of cardiac glycosides, saponins, tannins, reducing sugar and triterpene steroids in the plant extract (14).

Harpagophytum procumbens

Harpagophytum procumbens DC (Pedaliaceae) is widely used in South African traditional medicine for the treatment, management and/or control of a variety of human ailments. In a study the anticonvulsant activity of *Harpagophytum procumbens* secondary root aqueous extract (HPE, 50–800 mg/kg i.p.) against pentylenetetrazole, picrotoxin and bicuculline induced seizures in mice were evaluated. Like the reference anticonvulsant agents (Phenobarbitone and diazepam), *H. procumbens* secondary root aqueous extract (HPE, 100–800 mg/kg i.p.) significantly ($P < 0.05$–0.001) delayed the onset of, and antagonized, pentylenetetrazole induced seizures. The plant's extract (HPE, 100–800 mg/kg i.p.) also profoundly antagonized picrotoxin induced seizures, but only partially and weakly antagonized bicuculline induced seizures. Although the data obtained in the present study do not provide conclusive evidence, it would appear that *H. procumbens* secondary root aqueous extract produces its anticonvulsant activity by enhancing GABAergic neurotransmission and/or facilitating GABAergic action in the brain. In general, the average onset of convulsion was delayed, while the average duration of convulsion was

markedly reduced. The plant's extract also depressed the central nervous system (CNS). It is, therefore, thought that the anticonvulsant property of the herb may be linked, at least in part, to its ability to depress the central nervous system. However, this data shown that *H. procumbens* secondary root aqueous extract possesses anticonvulsant activity, and thus lend pharmacological support to the suggested folkloric, ethnomedical uses of the plant's extract in the treatment, management and/or control of epilepsy and childhood convulsions in some rural communities of South Africa (15).

Mimosa pudica

The decoction of *Mimosa pudica* leaves given intraperitoneally at dose of 1000–4000 mg/kg protected mice against pentylentetrazol and strychnine-induced seizures. *M. pudica* had no effect against picrotoxin-induced seizures. It also antagonized *N*-methyl-D -aspartate- induced turning behavior. These properties justified its use in African traditional medicine (16).

Cyperus articulatus

The methanolic extract of rhizomes of *Cyperus articulatus*, a plant used in traditional medicine in Africa and Latin America for many diseases, possesses anticonvulsant activity in mice. Methanolic extract protected mice against maximal electroshock (MES)- and pentylenetetrazol (PTZ)-induced seizures. It also delayed the onset of seizures induced by isonicotinic acid hydrazide and strongly antagonized *N*-methyl-D -aspartate-induced turning behavior. The ED_{50} for protection against seizures was 306 (154–541) mg/kg intraperitoneally (i.p.) for the PTZ test and 1005 (797–1200) mg/kg i.p. for the MES test. The ED_{50} of methanolic extract against *N*-methyl-D -aspartate-induced turning behavior was 875 (623–1123) mg/kg i.p. *C. articulatus* L. methanolic extract protected 54% of mice from seizures induced by strychnine at the dose of 1000 mg/kg i.p. but had no or a moderate effect only against picrotoxin- or bicuculline-induced seizures. With these effects, the rhizome of *C. articulatus* L. possesses anticonvulsant properties in animals that might explain its use as a traditional medicine for epilepsy in Africa (17).

Sutherlandia frutescens

Aerial parts of *Sutherlandia frutescens* R. BR. (Fabaceae) are extensively used in South African traditional medicines for the treatment, management and/or control of an array of human ailments, including childhood convulsions and epilepsy. The anticonvulsant property of the plant's shoot aqueous extract (25–400 mg/kg i.p.) against pentylenetetrazole, picrotoxin and bicuculline induced seizures in mice was observed. Like the reference antiseizure drugs (Phenobarbitone and diazepam), *S. frurescens* shoot aqueous extract (50–400 mg/kg i.p.) significantly delayed ($p < 0.05$–0.001) the onset of, and antagonized, pentylenetetrazole induced seizures. The plant's shoot aqueous extract (50–400 mg/kg i.p.) also profoundly antagonized picrotoxin induced seizures, but only weakly antagonized bicuculline induced seizures. Although the data do not provide conclusive evidence, it appears that *S. frurescens* shoot aqueous extract (SFE) produces its antiseizure effect directly by acting like GABA, or indirectly by enhancing GABAergic neurotransmission and/or action in the brain. The animal study results suggested that the herb may be used as a natural supplementary remedy in the management, control and/or treatment of childhood convulsions and epilepsy. In conclusion, the findings of this study indicate that *S. frurescens* shoot aqueous extract possesses anticonvulsant activity, and thus lend pharmacological credence to the suggested folkloric, ethnomedical uses of the herb in the management or treatment of childhood convulsions and epilepsy in some rural communities of South Africa (18).

Casimiroa edulis

A single dose of *Casimiroa edulis* aqueous and ethanolic extracts in combination with propyleneglycol (Pg), phenytoin (Phen) and phenobarbital (Phb) was orally given to adult male Wistar rat groups. Thereafter, all groups were assayed for protection against maximal electroshock (MES) and pentylenetetrazole (METsc) seizure inducing tests at hourly intervals throughout 8 h. For MES, a maximal protection of 70% at the 2nd and 4th h of E-OH doses occurred. That of Phen, Phb and Pg was 80, 90 and 10% at the 8th, 6th and 2nd h, respectively. The averaged values of the MES unprotected rats under AQ and E-OH extracts showed that a shortened reflex duration as well as a delayed latency and uprising times occurred. On the other hand, just an enlarged latency and no protection against METsc device in aqueous and ethanolic were observed. Phen and Phb maximal protection was 80 and 100% at the 4th and 6th hour against METsc. Thus, aqueous extract is tenfold more potent anticonvulsive extract than E-OH against MES (19).

Lippia alba

Lippia alba liquid and spray-dried extracts, containing the non-volatile fraction from the leaves, was investigated for The CNS activity. All mice were evaluated in the barbiturate-induced sleep test. Similarly, other groups of mice were submitted to convulsions induced by pentylenetetrazol (PTZ). In conclusion, it demonstrated that the non-volatile fraction of *L. alba*, extracted in ethanol 80% (v/v), presents sedative and myorelaxant effects and that, among the tested extracts, this presents the highest flavonoid content(66 mg/100 g, expressed in apigenin) (20).

Desmodium adscendens

Pharmacological effects of the ethanolic extract of the leaves of *Desmodium adscendens* (Papillionaceae), a medicinal plant in the African traditional medicine, on the central nervous system were evaluated. *D. adscendens* suppressed the tonic phase of convulsion and mortality induced by pentylenetetrazole (PTZ) in mice. In addition, the plant extract delayed the onset of PTZ forelimb clonus, and generalized limbic seizures induced by kainic acid. In contrast, the plant extract did not affect either tonic convulsion induced by maximal electroshock in mice or the progression of limbic seizures towards the status epilepticus in rats (21).

Unmadnashak Ghrita

'Unmadnashak Ghrita' (UG) is a ayurvedic formulation containing *Ferula narthex* (6 g), *Gardenia gummifera* (6 g), *Ellataria cardamom* (6 g), *Bacopa monneri* (6 g), and cow's

ghee (clarified butter fat) (76 g). Neuropharmacological activities of UG were evaluated for its gross behavioural effect, pentobarbitone sleeping time, spontaneous locomotor activity, antagonism to amphetamine induced hyperlocomotor activity, analgesic activity by tail flick test, rota-rod performance (motor coordination test), maximal electroshock (MES) induced seizures, and pentylenetetrazol (PTZ) induced convulsions in mice. The formulation showed CNS-depressant activity in gross behavioral test, potentiated pentobarbitone sleeping time and there was significant decrease in spontaneous locomotor count in mice. The formulation also antagonized the behavioral effects of CNS-stimulant drug amphetamine, and showed analgesic effect in mice. The formulation also protected mice from MES and PTZ induced convulsions. These results suggested that UG has CNS-depressant and anticonvulsant activity in mice (22).

Butea monosperma

The bioassay-guided fractionation of dried flowers of *Butea monosperma* (BM) was carried out to isolate the active principle responsible for its anticonvulsant activity. The anticonvulsive principle of *B. monosperma* was found to be a triterpene (TBM) present in the n-hexane: ethyl acetate (1:1) fraction of the petroleum ether extract. TBM exhibited anticonvulsant activity against seizures induced by maximum electroshock (MES), seizures induced by pentylenetetrazol (PTZ), electrical kindling, and the combination of lithium sulfate and pilocarpine nitrate (Li-Pilo). However, TBM was not effective against seizures induced by strychnine and picrotoxin. TBM exhibited depressant effect on the central nervous system. Further studies are required to investigate its usefulness in the treatment of epilepsy (23).

Hypoxis hemerocallidea

Extracts of *Hypoxis hemerocallidea* (Hypoxidaceae) corm (popularly known as 'African potato') are extensively used in South African traditional medicines for the treatment, management and/or control of an array of human ailments, including childhood convulsions and epilepsy. Anticonvulsant activity of the plant's corm aqueous extract (APE, 50-800 mg/kg i.p.) against pentylenetetrazole, picrotoxin and bicuculline induced seizures in mice were examined. Like the reference (Phenobarbitone and diazepam) antiseizure drugs used, *Hypoxis hemerocallidea* corm aqueous extract significantly delayed the onset of, and antagonized, pentylenetetrazole induced seizures. The plant's corm aqueous extract (APE, 100-800 mg/kg i.p.) also profoundly antagonized picrotoxin induced seizures, but only weakly antagonized bicuculline induced seizures. It would appear that 'African potato' aqueous extract (APE) produces its antiseizure effect by enhancing GABAergic neurotransmission and/or action in the brain. The results indicate that APE possesses anticonvulsant activity in the mammalian experimental model used and, therefore, tend to suggested that the herb may be used as a natural supplementary remedy in the management, control and/or treatment of childhood convulsions and epilepsy. In conclusion, *Hypoxis hemerocallidea* corm aqueous extract possesses anticonvulsant activity, and thus lend pharmacological credence to the suggested folkloric, anecdotal ethnomedical uses of the herb in the management of childhood convulsions and epilepsy in some rural communities of South Africa (24).

Persea americana

Various morphological parts of *Persea americana* Mill (Lauraceae) (avocado) are widely used in African traditional medicines for the treatment, management and/or control of a variety of human ailments, including childhood convulsions and epilepsy. The anticonvulsant effect of the plant's leaf aqueous extract against pentylenetetrazole, picrotoxin and bicuculline induced seizures in mice were evaluated. Like the reference anticonvulsant (Phenobarbitone and diazepam) agents used, *Persea americana* leaf aqueous extract significantly delayed the onset of, and antagonized, pentylenetetrazole induced seizures, picrotoxin induced seizures, but only weakly antagonized bicuculline induced seizures. It would appear that 'avocado' leaf aqueous extract (PAE) produces its anticonvulsant effect by enhancing GABAergic neurotransmission and/or action in the brain. This data indicate that *Persea americana* leaf aqueous extract possesses an anticonvulsant property, and thus lends pharmacological credence to the suggested ethnomedical uses of the plant in the management of childhood convulsions and epilepsy (25).

Egletes viscose

The essential oil from flower heads of *Egletes viscose* L. was investigated for possible antinociceptive, anticonvulsant effects. It was found to possess a significant dose-dependent analgesic activity as assessed by acetic acid writhing and formalin tests and also an anticonvulsant activity against convulsions induced by pentylenetetrazol in mice (26).

Artemisia verlotorum

The anticonvulsive activity of the crude hydroalcoholic extract (HE) of *Artemisia verlotorum* (Compositae) was analyzed as a part of a psychopharmacological screening of this plant. HE (2 g/kg) prevented the onset of electroshock and pentylenetretazole induced convulsions and also increased the latencies to convulsions induced by 3-mercaptopropionic acid and pilocarpine in mice. These findings supported the popular use of *Artemisia verlotorum* as an anti-convulsant and analgesic (27).

Screening Of Plants Used In Southern Africa For Epilepsy And Convulsions In The $Gaba_a$-Benzodiazepine Receptor Assay

A number of plants are traditionally used to treat mental diseases in South Africa. Aqueous and ethanol extracts of plants that are traditionally used to treat against epilepsy and convulsions were tested in the $GABA_A$-benzodiazepine receptor binding assay, where the binding of ^{3}H-Ro 15-1788 (flumazenil) to the benzodiazepine site is measured. The $GABA_A$-benzodiazepine receptor complex is involved in epilepsy and convulsions. The most active extracts were the ethanolic leaf extracts of *Rhus tridentata*, *Rhus rehmanniana* and *Hoslundia opposita* and the ethanolic corm extract of *Hypoxis colchicifolia*, which all showed good dose-dependent activity (Table 1) (28).

PLANTS USED TO TREAT EPILEPSY BY TANZANIAN TRADITIONAL HEALERS

A cross-sectional study performed in Temeke District (Dar es Salaam, Tanzania) showed that 5.5% of the traditional healers have knowledge for the treatment of epilepsy. Of the 100 healers interviewed, 30 (30%) believed that epilepsy was caused by witchcraft, while 19 (19%) thought epilepsy has a genetic origin which can be inherited. Other healers thought epilepsy can be caused by head injury or malaria (24%), and the remaining 27% did not know the cause. Most of the healers (92%) could present an accurate account on the symptoms of the disease, including dizziness, loss of consciousness, abrupt falling down, frothing from the mouth, loss of memory, biting of the tongue, confusion, and restlessness. They showed competence in the treatment of the disease, whereby 60 plants that are commonly used were mentioned. *Abrus precatorius* L. (Leguminosae) *Clausena anisata* (Willd.) Oliv (Rutaceae) and *Hoslundia opposita* Vahl (Lamiaceae), which are among the plants mentioned, have proven anticonvulsant activity, while a few other species on their list have been reported to be useful in the treatment of epilepsy. Biological testing of these plants, using different models of convulsions is, suggested (Table 2) (29).

Calotropis gigantea

Alcoholic extract of peeled roots of *Calotropis gigantea* R.Br. (Asclepiadaceae) was tested orally in albino rats at the dose level of 250 and 500 mg/kg for CNS activity. Significant anticonvulsant activity was seen as there was a delay in the onset of pentylenetetrazole induced convulsions as well as decrease in its severity (30).

Clitoria ternatea

The investigation was carried out to determining the spectrum of activity of the methanolic extract of *Clitoria ternatea* (CT) on the CNS. The CT was studied for its effect on cognitive behavior, anxiety, depression, stress and convulsions induced by pentylenetetrazol (PTZ) and maximum electroshock (MES). To explain these effects, the effect of CT was also studied on behavior mediated by dopamine (DA), noradrenaline, serotonin and acetylcholine. It reduced the convulsing action of PTZ and MES. The extract exhibited tendency to reduce the intensity of behavior mediated via serotonin and acetylcholine. Further studies are necessary to isolate the active principle responsible for the activities and to understand its mode of action (31).

Vitex-negundo

Maximal electroshock seizures (MES) in albino rats and pentylenetetarazole (PTZ) induced seizures in albino mice were used to study anticonvulsant activity of *Vitex-negundo* leaf extract. The ethanolic leaf extract of *Vitex-negundo* was administered orally in both the experimental models and the effects were compared with diphenylhydantoin in MES method and valporic acid in PTZ induced seizures method as standard control respectively. The *Vitex-negundo* in the doses (250, 500 and 1000 mg/kg, p.o) did not show protection against MES to any significant extent but significant post-ictal depression was observed in the dose of 1000 mg/kg body weight in comparison to control. However, sub-protective dose of test drug (100 mg/ kg, p.o) potentiated the anticonvulsant action of diphenylhydantoin. The test drug in the dose (1000 mg/kg, po) showed 50% protection in clonic seizures and 24-hour mortality against PTZ induced seizures. It also decreased number and duration of convulsions significantly. *Vitex-negundo* potentiated anticonvulsant activity of valporic acid. The anticonvulsant activity of *Vitex-negundo* has not been found equi-effective with standard drugs. These findings suggest that *Vitex-negundo* possesses anticonvulsant activity particularly against PTZ induced convulsions. Moreover, the potentiation of diphenylhydantoin and valporic acid by *Vitex-negundo* indicates that it may be useful as an adjuvant therapy along with standard anticonvulsants and can possibly lower the requirement of diphenylhydantoin and valporic acid (32).

Cymbopogon winterianus

Cymbopogon winterianus (Poaceae) is used for its analgesic, anxiolytic and anticonvulsant properties in Brazilian folk medicine. This report aimed to perform phythochemical screening and to investigate the possible anticonvulsant effects of the essential oil (EO) from fresh leaves of *C. winterianus* in different models of epilepsy. The phytochemical analysis of EO showed presence of geraniol (40.06%), citronellal (27.44%) and citronellol (10.45%) as the main compounds. A behavioral screening demonstrated that EO (100, 200 and 400 mg/kg; ip) caused depressant activity on CNS. When administered concurrently, EO (200 and 400 mg/kg, ip) significantly reduced the number of animals that exhibited PTZ- and PIC-induced seizures in 50% of the experimental animals. Additionally, EO (100, 200 and 400 mg/kg, ip) significantly increased the latencies of clonic seizures induced by STR. These results demonstrated a possible activity anticonvulsant of the EO (33).

CONCLUSION: It is now quiet pertinent that commonly available synthetic anticonvulsants does not adequately meet patient treatment demands, herbal drugs exhibiting promising anticonvulsant activity by enhancing GABAergic neurotransmission/or action in the brain or GABAergic and glutaminergic systems or alteration of glutamate receptor binding and gene expression of NMDA R1 in hippocampus of temporal lobe. From the reported studies it was concluded that few herbal drugs are more potential and many are having fewer side effects. Apart from the above discussed mode of action there are many other plants which work on other mechanism of action like blockade of sodium & calcium channels, inhibition of glutamate and some other lesser known mechanism. Also we can conclude that there is a strong direct correlation between the ethnopharmacological usage with that of scientifically proven claims which justify and hence supports the traditional therapy not only in our country but also in other countries. Since therapeutic alternative offered by knowledge of ethnopharmacology have not yet been properly and fully explored there is still promising potential in plant sources for obtaining “leads” and “hits” for suitable drug development candidate.

REFERENCES:

1. W. A. Hoogerwerf, P. J. Pasricha. Drugs Effective in the Therapy of The Epilepsy. The Pharmacological Basis of Therapeutics. The Mc Graw Hill, New York, USA; 521-548 (2001).

2. M. Nisar, I. Khan, S. U. Simjee, A. H.Gilani, Obaidullah and H. Perveen. Anticonvulsant, analgesic and antipyretic activities of *Taxus wallichiana* Zucc.*Journal of Ethnopharmacology*. **116**: 490-494 (2008).
3. V. S. Rao, A. Rao and K. S. Karanth. Anticonvulsant and neurotoxicity profile of *Nardostachys jatamansi* in rats. *Journal of Ethnopharmacology*.**102**: 351-356 (2005).
4. H. G. Park, S. Y. Yoon, J. Y. Choi, G. S. Lee, J. H. Choi, C. Y. Shin, K. H. Son,
Y. S. Lee, W. K. Kim, J.H. Ryu, K. H. Ko and J. H. Cheong. Anticonvulsant effect of wogonin isolated from *Scutellaria baicalensis*. *European Journal of Pharmacology*. **574**: 112-119 (2007).
5. M. Nassiri-Asl, S. Shariati-Rad and F. Zamansoltani. Anticonvulsive effects of intracerebroventricular administration of rutin in rats. *Progress in Neuro- Psychopharmacology and Biological Psychiatry* . **32**: 989-993 (2008).
6. H. Pérez-Saad and T. María. Buznego Behavioral and antiepileptic effects of acute administration of the extract of the plant *Cestrum nocturnum Lin* (lady of the night). *Epilepsy & Behavior*. **12**: 366-372 (2008).
7. R. Khan, A. Krishnakumar and C.S. Paulose. Decreased glutamate receptor binding and NMDA R1 gene expression in hippocampus of pilocarpine-induced epileptic rats: Neuroprotective role of *Bacopa monnieri* extract. *Epilepsy & Behavior*.**12**: 54-60 (2008).
8. N. J. Sucher. Insights from molecular investigations of traditional Chinese herbal stroke medicines: Implications for neuroprotective epilepsy therapy. *Epilepsy & Behavior.* **8**: 350-362 (2006).
9. A.O. Ayoka, R. O. Akomolafe, E. O. Iwalewa, M.A. Akanmu and O.E. Ukponmwan. Sedative, antiepileptic and antipsychotic effects of *Spondias mombin* L. (Anacardiaceae) in mice and rats. *Journal of Ethnopharmacology*. **103**: 166-175 (2006).
10. O. Olufunmilayo. Adeyemi, K. Omoniyi,Yemitan and O. Olayemi. Adebiyi Sedative and anticonvulsant activities of the aqueous root extract of *Sanseviera liberica* Gerome & Labroy (Agavaceae). *Journal of Ethnopharmacology*. **113**: 111-114 (2007).
11. S.K. Kulkarni and A. Dhir. *Somnifera*: An Indian ginseng. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*.**32**: 1093-1105 (2008).
12. M. Saberi, A. Rezvanizadeh and A. Bakhtiarian. The antiepileptic activity of *Vitex agnus castus* extract on amygdala kindled seizures in male rats. *Neuroscience Letters*. **441**: 193-196 22 (2008).
13. E. Bienvenu , G.J. Amabeoku , P.K. Eagles , G. Scott , E.P. Springfield . Anticonvulsant activity of aqueous extract of *Leonotis leonurus*. *Phytomedicine*. **9**:217-23 (2002).
14. G.J. Amabeokua, I. Greenb and J. Kabatendea. Anticonvulsant activity of *Cotyledon orbiculata* L. (Crassulaceae) leaf extract in mice. *Journal of Ethnopharmacology*. **112**: 101-107 (2007).
15. M. Ismail. Mahomed and A.O. John Ojewole. Anticonvulsant activity of *Harpagophytum procumbens* DC [Pedaliaceae] secondary root aqueous extract in mice. *Brain Research Bulletin*. **69**: 57-62 (2006).
16. E. Ngo Bum, D. L. Dawack, M. Schmutz, A. Rakotonirina, S. V. Rakotonirina, C. Portet, A. Jeker, H. -R. Olpe and P. Herrling. Anticonvulsant activity of *Mimosa pudica* decoction. *Fitoterapia.* **75**:309-14 (2004).
17. E. Ngo Bum, M. Schmutz, C. Meyer, A. Rakotonirina, M. Bopelet, C. Portet, A. Jeker, S. V. Rakotonirina, H. R. Olpe and P. Herrling. Anticonvulsant properties of the methanolic extract of *Cyperus articulatus* (Cyperaceae). *Journal of Ethnopharmacology*. **76**: 145-150 (2001).
18. J. A.O. Ojewole. Anticonvulsant property of *Sutherlandia frutescens* R. BR. (variety *Incana* E. MEY.) [Fabaceae] shoot aqueous extract. *Brain Research Bulletin*. **75**: 126-132 (2008).
19. P. Garzón-De la Mora, P. M. García-López, J. García-Estrada, A. Navarro-Ruíz, T. Villanueva-Michel, L. Ma. Villarreal-de Puga and J. Casillas-Ochoa *Casimiroa edulis* seed extracts show anticonvulsive properties in rats. *Journal of Ethnopharmacology*. **68**: 275-282 (1999).
20. M. Zétola, T. C. M. De Lima, D. Sonaglio, G. González-Ortega, R. P. Limberger, P. R. Petrovick and V. L. Bassani. CNS activities of liquid and spray-dried extracts from *Lippia alba* Verbenaceae (Brazilian *false melissa*). *Journal of Ethnopharmacology.* **82**: 207-215 (2002).
21. P. N'gouemo, M. Baldy-Moulinier and C. Nguemby. Effects of an ethanolic extract of *Desmodium adscendens* on central nervous system in rodents Bina. *Journal of Ethnopharmacology*. **52**:77-83 (1996).
22. G. S. Achliya, S. G. Wadodkar and A. K. Dorle, Evaluation of sedative and anticonvulsant activities of Unmadnashak Ghrita. *Journal of Ethnopharmacology.* **94**: 77-83 (2004).
23. V. S. Kasture, S. B. Kasture, C. T. Chopde *Anticonvulsive ativity of Butea monosperma* flowers in laboratory animals. *Pharmacol Biochem Behav*. **72**: 965-972 (2002).
24. J. A. Ojewole Anticonvulsant activity of *Hypoxis hemerocallidea* Fisch. & C. A. Mey. (Hypoxidaceae) corm ('African potato') aqueous extract in mice. *Phytother Res.* **22**: 91-96 (2008).
25. J. A. Ojewole , G. J. Amabeoku. Anticonvulsant effect of *Persea americana* Mill (Lauraceae) (Avocado) leaf aqueous extract in mice. *Phytother Res.* **20**:696-700 (2006).
26. L. M. F. Souza, F. A. Santos, V. S. N. Rao, J. J. C. Sidrim , F. J. A. Matos , M. I. L. Machedo , E. R. Silveira. Antinociceptive, anticonvulsant and antibacterial effects of the essential oil from the flower heads of *Egletes viscose*. *Phytotherapy Research*. **12**: 28 – 31 (1998).
27. T. C. M. de Lima, G. S. Morato, R. N. Takahashi Evaluation of the Central Properties of *Artemisia verlotorum*. *Planta Med*. **59**: 326-329 (1993).
28. J. Risa, A. Risa, A. Adsersen, B. Gauguin, G. I. Stafford, J. van Staden and A. K. Jäger. Screening of plants used in southern Africa for epilepsy and convulsions in the $GABA_A$-benzodiazepine receptor assay. *Journal of Ethnopharmacology.* **93**:177-182 (2004).
29. Mainen J. Moshi, Godeliver A.B. Kagashe and Zakaria H. Mbwambo. Plants used to treat epilepsy by Tanzanian traditional healers. *Journal of Ethnopharmacology*. **97**(2): 327-336(2005).
30. A. Argal and A. K. Pathak CNS activity of *Calotropis gigantea* roots. *Journal of Ethnopharmacology*. **106**: 142-145(2006).
31. N. N. Jain, C. C. Ohal, S. K. Shroff, R. H. Bhutada, R. S. Somani, V. S. Kasture and S. B. Kasture. *Clitoria ternatea* and

the CNS. *Plants and the Central Nervous System*. **75**: 529-536 (2003).

32. V. R. Tandon and R. K. Gupta. An Experimental Evaluation of Anticonvulscent Activity of *Vitex negundo*. *Indian J Physiol Pharmacol*. **49**: 199–205 (2005).
33. L.J. Quintans-Ju´ nior, T.T. Souza, B.S. Leite, N.M.N. Lessa, L.R. Bonjardim, M.R.V. Santos, P.B. Alves, A.F. Blank, A.R. Antoniolli. Phythochemical screening and anticonvulsant activity of *Cymbopogon winterianus* Jowitt (Poaceae) leaf essential oil in rodents. *Phytomedicine*. **15**:619–624 (2008).