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Herbal and synthetic approaches for the treatment of epilepsy

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ABSTRACT

The term epilepsy is collectively designated for a group of chronic central nervous system disorders characterized by spontaneous occurrence of seizures generally associated with the loss of consciousness and body movements (convulsions). Anticonvulsant drugs are used to control the convulsions by inhibiting the discharge and then producing hypnosis. Various synthetic drugs, viz. phenytoin (PHT), diazepam, valproate (VPA), leviteracetam, etc., are used for the treatment. These agents have a new spectrum of efficacy and novel adverse effects. They also represent an enormous escalation of costs. At present, herbal therapies are tried by patients in developing as well as developed countries for control of seizures or adverse effects from antiepileptic drugs, or for general health maintenance. There are number of synthetic 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.

Key words: Convulsion, epilepsy, herbal treatment, seizures

INTRODUCTION

The term "epilepsy" is derived from Greek word "epilambanein", which means "to seize upon" or "to attack". In this modern world, epilepsy is one of the most frequent neurodegenerative diseases.[1] Epilepsy is a condition in which a person has recurrent seizures. Seizure can defined as an abnormal, disorderly discharging of nerve cells of brain; resulting in a temporary disturbance of motor, sensory, or mental function.[2] Epilepsy is the most common neurological condition affecting people of all ages, race, and social class. There are 50 million people with epilepsy in the world, of which up to 75% live in resource-poor countries with less or no access to medical treatment.[3]

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Epilepsy is not curable, but can be controlled with anticonvulsant which prevent the seizures or lessen their intensity.[4] The discovery of novel antiepileptic drugs relies upon the preclinical employment of animal models to establish efficacy and safety prior to the introduction of the antiepileptic drugs (AEDs) in human volunteers.[5] In last 15 years, a new generation antiepileptic drugs has been introduced for the management of seizures. With the development, the concept of optimum therapy for seizures has evolved to include complete control of seizures, absence of bothersome side effects, and an emphasis on maximizing quality of life.[6] Still today, majority of person with epilepsy around the world not receiving the treatment, largely because of their lack of access to physicians and the costs of AEDs.[7]

It is estimated that there are more than 10 million people with epilepsy in our country.[8] AEDs are widely used not only for the treatment of epilepsy, but also for additional indications such as bipolar disorder, migraine, and chronic pain. Because these drugs are commonly prescribed for long periods,

many patients will require treatment with other agents for the management of concomitant or intercurrent conditions. In this setting, the potential for drug interactions is considerable. The increasing use of over-the-counter medication creates a further source of potential clinically significant interactions.[9]

Over thousands of years, people with epilepsy have used a variety of botanicals and herbs, hereafter referred to simply as herbal therapies (although no clinical benefit is implied by this term).[7] Traditional systems of medicine are popular in developing countries and up to 80% of the population relies on traditional medicines for their primary healthcare needs. Several plants used for the treatment of epilepsy in different systems of traditional medicine have shown activity when tested on modern bioassays for the detection of anticonvulsant activity and many such plants remain to be scientifically investigated.[10]

TYPES OF EPILEPSY

Seizure can be differentiated in focal and generalized seizure epilepsy.[11]

Generalized seizures

- Convulsive (bilateral motor manifestations with or without loss of consciousness; "Grand mal" seizures)
  - Tonic-clonic
  - Tonic
  - Clonic
  - Myoclonic.
- Nonconvulsive (usually no motor component; consciousness impaired; "Petit mal" or absence seizures).

Partial seizures

- Simple partial (usually unilateral focal motor signs with no loss of consciousness; "Focal motor" seizures
- Complex partial (usually psychic symptoms with unusual behavior stereotypes; usually impaired consciousness; "Psychomotor" seizures)
- Partial seizures with secondary generalization (can occur with either simple partial or complex partial seizures).[12]

DIAGNOSIS AND TREATMENT

The neurochemistry of the seizure disorder is complex and not yet understood. Epilepsy may result from long lasting plastic changes in the brain affecting neurotransmitters release and transport, the properties of receptors and channels, regulation of gene expression, synaptic reorganization, and astrocyte activity. Initially, it was considered that ion channel alterations may cause the onset of the paroxysmal depolarization shifts that initiate epileptic activity. Recent studies on synaptic and nonsynaptic transmission, ion channels interactome, intracellular signaling pathways, and glia-neuron signaling suggest that many neurochemical pathways play an important role in seizure initiation, maintenance, and arrest.[13] In the past, the diagnosis of seizure disorders had been based on a clinical history, substantiated by eyewitness, and supplemented by investigations. Eyewitness descriptions are an integral part of diagnosis. They comprise past and family history, cognitive problems, and other illnesses causing or modifying seizure problems. The visual content of seizures is capable of being recorded by 24 h video monitoring, coupled with simultaneously linked electroencephalographic (EEG) recording. Radiological diagnosis has evolved from skull films and pneumoencephalograms (PEG) to computed axial tomography (CT scan), completely superseded by magnetic resonance imaging (MRI) with special sequences to highlight areas associated with the origin of seizures. Magnetic resonance angiogram (MRA) is not routinely employed to study a vascular etiology of seizures, but it may be used in the investigation of stroke which may be associated with seizures. Positron emission tomography (PET) has been developed, although it is extremely costly, and not available in all centers. Single photon emission tomography (SPECT), developed to a significant extent in Melbourne, has gained acceptance worldwide as an additional test, for localization of sites of origin of seizures. Once a firm diagnosis of epilepsy is made, a decision needs to be taken whether to start treatment. Two decades ago a single seizure in the absence of a demonstrable underlying cause, was often not treated. One current view is that seizures in the majority of patients are recurrent; hence they ought to be treated from the outset. However, 4050% of presenting seizures turn out to be isolated events. Certainly first seizures with specific EEG findings to allow seizure differentiation may indicate the need for early treatment. Those with clinical and positive MRI findings suggesting a high chance of recurrence, as in lesional focal epilepsy and symptomatic epilepsy, ought to be treated from the outset. There have been tremendous advances in surgery, both in the diagnostic and therapeutic approaches. Patients with focal epilepsy after a thorough trial of medical treatment can now be referred for diagnostic evaluation for possible resection of a

unilateral focus. In selected cases, palliation may be offered by callosal section in symptomatic generalized epilepsy. Intermittent vagal stimulation is another option for therapy, but the cost may be prohibitive for many sufferers, as the equipment cannot be reused, for risk of infection.[14]

OLDER GENERATION DRUGS

Carbamazepine

CBZ blocks voltage-dependent sodium channels, thereby limiting rapid, repetitive neuronal firing. CBZ is a first-line treatment for partial epilepsy, but is ineffective against, and may exacerbate, absence and myoclonic seizures.[15] To minimize CNS-related side effects; CBZ should be initiated at 100-200 mg daily and increased by 100-200 mg increments every 3-14 days as needed for seizure control, typically over 1-2 months. Hepatic metabolism is induced by CBZ.[16]

Phenytoin

PHT blocks voltage-dependent neuronal sodium channels and is a first-line treatment for partial onset and primary generalized tonic-clonic seizures. PHT is ineffective against myoclonic, atonic, and absence seizures.[17] In a nonurgent situation, oral treatment is often started at the anticipated maintenance dose, typically 300 mg/day administered either as a single dose or in two divided doses in adults (5-8 mg/kg/day in children).[18] PHT induces hepatic enzymes, reducing serum concentrations of other hepatically metabolized AEDs such as CBZ, valproate (VPA), lamotrigine (LTG), and topiramate (TPM), as well as hormonal contraceptives.[19]

Sodium valproate

Sodium VPA blocks voltage-dependent sodium channels, facilitates the effects of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), and reduces low threshold (T-type) calcium currents.[20] Sodium VPA is effective for virtually all seizure types.[21] Therapy is initiated with 500 mg once or twice daily, and titrated as needed for seizure control. An intravenous form allows for a loading dose and substitution for oral therapy when needed.[22]

Ethosuximide

ESM reduces T-type calcium currents in thalamic neurons. It is a first-line treatment for patients with absence seizures, but ineffective against myoclonic, primary generalized tonic-clonic, and partial onset seizures. The usual initial dose is 250-500 mg daily, with 250 mg dose increments over 2-3 weeks as needed for seizure control. Drug interactions are not a significant problem.[6]

Primidone

PRM is metabolized in the liver to phenobarbitol (PB) and another active compound, phenylethylmalonamide.[23] PRM is effective against partial onset and primary generalized tonic-clonic seizures. Dosing is usually initiated with 125 mg at bedtime, and increased by 125 mg every 3-5 days as needed for seizure control up to 1,500 mg daily. As with PB, abrupt discontinuation of PRM should be avoided. PRM induces hepatic metabolism.[24]

NEWER ANTIEPILEPTIC DRUGS

Gabapentin

Gabapentin (GBP) in clinical use since 1996 binds to the $\alpha 2\delta$ subunit of neuronal voltage-gated calcium channels, inhibiting calcium flow. Gabapentin is effective against partial onset seizures, but may exacerbate myoclonic and absence seizures. The typical initial dose is 300 mg daily, which is increased by 300 mg every 3 days, as needed for seizure control, to the maximum tolerated dose. There is no significant drug interactions. Because GBP is eliminated by the kidneys, patients with renal insufficiency require lower dosages and less frequent dosing.[25]

Lamotrigine

LTG is a sodium channel blocker that is effective against partial onset seizures and generalized seizure subtypes, though it has been reported to exacerbate myoclonic seizures.[26] Dosing is started at a low dose, 25-50 mg daily, and increased slowly. Starting dosages, subsequent increments, and target maintenance dosages are reduced in patients comedicated with VPA.[27,28]

Felbamate

FBM potentiates GABA-mediated inhibition, and blocks voltage-dependent sodium channels as well as the ionic channel at the *N*-methyl-d-aspartate receptor FBM is effective against partial onset seizures as well as generalized seizures. Dosing is titrated slowly over several weeks to minimize side effects.[29]

Levetiracetam

LEV binds to synaptic vesicle protein and has actions on neuronal GABA- and glycine-gated currents, as well as voltage-dependent potassium currents, though its exact mechanism of action is unknown. LEV is effective against partial onset seizures as well as

generalized seizure types, including myoclonic and absence seizures.[30] Dosing is initiated at 500-1,000 mg daily and titrated at 1,000 mg increments every 2 weeks as tolerated and needed for seizure control. There are no pharmacokinetic interactions with other drugs.[31]

Oxcarbazepine

OXC is the prodrug for its active metabolite, 10,11-dihydro-10-hydroxycarbazapine, which blocks voltage-dependent sodium channels, and modulates calcium and potassium currents. OXC is the 10,11 keto analogue of CBZ, and has a similar spectrum of efficacy against partial onset[30] and primary generalized tonic-clonic seizures. Dosage is usually initiated at 150-600 mg daily in adults and titrated every 1-2 weeks as needed to control seizures and as tolerated.[32]

Pregabalin

PGB binds with high affinity to the α2δ subunit of neuronal voltage-gated calcium channels and inhibits calcium flow, an action similar to GBP.[25] PGB is effective against partial onset seizures and is six to eight times more potent than GBP.[33] The usual initial dose is 150 mg daily, for add on therapy a twice daily application of PGB is recommended.[25]

Tiagabine

TGB inhibits neuronal and glial reuptake of GABA, which increases the availability of GABA to inhibit postsynaptic neurons.[34] TGB is effective against partial-onset seizures, but has been reported to rarely precipitate absence stupor.[35] Treatment is initiated with 4-8 mg daily, and increased weekly by 4-8 mg as needed for control of seizures and as tolerated.[36]

Topiramate

TPM blocks sodium channels and high voltage activated calcium channels, attenuates the effects of excitatory neurotransmitters, enhances GABAergic neurotransmission, and inhibits carbonic anhydrase, though the relevance of this last mechanism to its anticonvulsant effect is uncertain. TPM is used for partial-onset, primary generalized tonic-clonic, and myoclonic seizures. The initial dose is 25-50 mg daily, which is increased by 25-50 mg every 1-2 weeks as needed for seizure control.[37,38]

Zonisamide

ZNS blocks voltage-dependent sodium channels as well as T-type calcium channels, and inhibits carbonic anhydrase. ZNS is effective against partial-onset seizures and generalized seizure subtypes, tonic-clonic, tonic, atonic, atypical absence, and myoclonic seizures.[30,39] The recommended initial dose is 100 mg daily for adult patients and 2 mg/kg/day for children in two divided dosages. Because steady state is reached slowly, doses should be increased at 2 week intervals to the target maintenance dose [Table 1].[40]

Table 1: Common side effects of antiepileptic drugs

Drug/brand name/ dose/manufacturer	Side effect			Price (INR)/ tablet
	General side effects	Neurological side effects	Idiosyncratic reaction	
Carbamazepine Carbada (200 mg) Cadila	Nausea, vomiting, diarrhea, hyponatremia, rash, pruritus, fluid retention	Drowsiness, dizziness, blurred or double vision, lethargy, headache	Agranulocytosis, Stevens-Johnson syndrome, aplastic anemia, hepatic failure, dermatitis-rash, serum sickness, pancreatitis	13/6
Lamotrigine Lamitor (100) Torrent pharma	Rash, nausea	Dizziness, vertigo, somnolence	Stevens-Johnson syndrome or lyell syndrome, hypersensitivity syndrome	152.40/10
Felbamate -	Nausea, vomiting, anorexia, weight loss	Insomnia, dizziness, headache, ataxia	Aplastic anemia, hepatic failure	-
Levetiracetam Levacetam (250) Micro Labs	Anorexia	Somnolence, asthenia, dizziness, headache, nervousness, double vision, skin reaction	NA	49/10
Oxcarbazepine Oxetol (150) Sun pharma	Nausea, vomiting, hyponatremia, rash	Drowsiness, dizziness, headache, double vision, ataxia	Dermatitis-rash, Stevens-Johnson syndrome, toxic epidermal necrolysis	41/10
Pregabalin Avertz (75) Dr. Reddy's	Weight gain, peripheral edema	Dizziness, somnolence, asthenia, headache, ataxia	-	80/10
Tiagabine -	-	Dizziness, weakness, asthenia, ataxia, nervousness, tremor, somnolence	-	-
Topiramate Nextop (100) Torrent	Anorexia, weight loss	Tremor	Agranulocytosis, Stevens-Johnson syndrome, aplastic anemia,	158/10

Table 1: Common side effects of antiepileptic drugs

Drug/brand name/ dose/manufacturer	Side effect			Price (INR)/ tablet
	General side effects	Neurological side effects	Idiosyncratic reaction	
			hepatic failure, dermatitis-rash, serum sickness	
Zonisamide Zonicare (100) Abbott	Anorexia	Dizziness, ataxia, fatigue, somnolence, confusion	Nephrolithiasis, oligohydrosis, and hyperthermia	94/10
Phenytoin Dilantin (100 mg) Pfizer	Gingival hypertrophy, body hair increase, rash, lymphadenopathy	Confusion, slurred speech, double vision, ataxia, neuropathy (with long-term use)	Agranulocytosis, Stevens-Johnson syndrome, aplastic anemia, hepatic failure, dermatitis-rash, serum sickness	168.28/100
Valproate Epilex (200) Abbott	Weight gain, nausea, vomiting, hair loss, easy bruising	Tremor	Agranulocytosis, Stevens-Johnson syndrome, aplastic anemia, hepatic failure, dermatitis-rash, serum sickness	25.75/10
Ethosuximide Zarontin (250) -	Nausea, vomiting	Sleep disturbances, hyperactivity	Agranulocytosis, Stevens-Johnson syndrome, aplastic anemia, hepatic failure, dermatitis-rash, serum sickness	-
Gabapentin Neurontin (300) Pfizer	-	Somnolence, dizziness, ataxia	-	312.87/10

INR: Indian rupee

PRINCIPLE

The AED is generally started at a low dosage and slowly titrated to the maximum-tolerated dose. If the first AED is unsuccessful because of ineffectiveness or side effects, then a second AED, also appropriate for the target seizure type (s), is generally prescribed. The second AED should be titrated to a tolerable and effective dosage before the first AED is tapered. In general, it is preferable to maintain a patient on a single AED rather than combinations of AEDs because compliance is enhanced, overall medication costs are usually less, and there are generally fewer idiosyncratic reactions, teratogenic effects, and side effects (though not invariably). Nonetheless, some patients do better on combinations of AEDs than on individual agents.[6]

HERBAL DRUGS USED IN TREATMENT OF EPILEPSY

Widespread and increasing interest in complementary and alternative medicines (CAMs), including herbal medicines. Herbal medicine is an area of CAM that is readily amenable to empirical research. Numerous herbal medicines have effects in the central nervous system and on hepatic metabolism, and thus have at least the theoretical potential for affecting seizures in patients with epilepsy and interacting with some antiepileptic medications.[41]

Nardostachys jatamansi (Jatamanasi)

The roots and the rhizomes of *N. jatamansi* DC. (Valerianaceae) mentioned in Ayurveda have been used to treat epilepsy, hysteria, syncope, and mental weakness. The ethanol extract of *N. jatamansi* considerably increased the seizure threshold in the experimental model of generalized tonic-clonic seizures with very low neurotoxic effect.[42]

Cotyledon orbiculata (seredile, plakkie, imphewula)

C. orbiculata L. (Crassulaceae) is reported that the juice has been used to treat epilepsy. However, traditional medicine practitioners in the Western Cape Province, South Africa use the infusion of the fleshy leaves for the treatment of epilepsy (oral communication). The leaves of *C. orbiculata* contain saponins, which may be of triterpenoid type, and the triterpene steroid present in *Cotyledon orbiculata* might contribute to the anticonvulsant activity of the plant.[43]

Laurus nobilis

L. nobilis Linn. (Lauraceae) the leaves of this plant have been used to treat epilepsy, neuralgia, and Parkinsonism. Pharmacological studies have demonstrated the anesthetic, hypothermic, muscle relaxant, and anticonvulsant activity of eugenol and methyleugenol and also antistress effect of eugenol. Furthermore, some analogs of α-pinene prevent the audiogenic seizures in susceptible rats.[44]

Bacopa monnieri (Bramhi)

B. monnieri, an Indian herbal drug, reputed nootropic plant. Commonly used to treat asthma, epilepsy, insanity, and hoarseness. It is a major constituent of medhya rasayana formulations.[45] *B. monniera* 300 mg/kg (oral) body weight/day 15 days treatment

to epileptic rat prevents the occurrence of seizures, thereby reducing the impairment on peripheral nervous system.[46]

Rhizoma Pinelliae

It is tuber of *Rhizoma ternate* (Thumb, Family: Araceae). The anticonvulsant action was widely evaluated to investigate the sedation/hypnotic drugs. The study showed ethanol fraction from Rhizoma Pinelliae Praeparatum (EFRP) could reduce the rate of nikethamide (NKTM)-induced convulsion death and prolong the latency, but not affect the convulsion latency which suggested that EFRP had the potential to modify the course of convulsive episodes and interfere in seizure threshold and/or block seizure propagation. It provided pharmacological supports for the use of Rhizoma Pinelliae Praeparatum on treatment of insomnia and central nervous disorders.[47]

Taxus wallichiana (Himalayan Yew)

T. wallichiana Zucc. (Himalayan Yew) is often used in epilepsy. The genus Taxus (Taxaceae) is well-known for the famous anticancer agent. Leaves of the plant are used to make herbal tea for indigestion and epilepsy. Anticonvulsant effect of *T. wallichiana* was compared with that produced by the GABA-A agonist diazepam, a potent antiepileptic drug, highly effective to prevent convulsions induced by PTZ.[48]

Sutherlandia frutescens (umwele, cancerbush)

Aerial parts of *S. frutescens* R. BR. (Fabaceae) are extensively used in childhood convulsions and epilepsy *S. frutescens* shoot aqueous extract (SFE, 50-400 mg/kg intraperitoneally (i.p.)) significantly delayed the onset of, and antagonized, pentylenetetrazole (PTZ)-induced seizures. The plant's shoot aqueous extract (SFE, 50-400 mg/kg i.p.) also profoundly antagonized picrotoxin (PCT)-induced seizures.[49]

Ficus platyphylla (Dell-holl)

F. platyphylla (Moraceae) is Nigerian traditional medicine to treat psychoses, depression, epilepsy, pain, and inflammation for many years; the crude methanol extract of *F. platyphylla* stem-bark contains sedative principles with potential neuroleptic, analgesic, and anti-inflammatory properties. Since saponins, which form the major components of the crude extract are believed to have profound central nervous system activities.[50]

Scutellaria baicalensis (Skullcaps)

S. baicalensis (Lamiaceae) is one of the most important medicinal herbs in traditional Korean medicine. Flavonoids from *S. baicalensis* may exert pharmacologically and clinically important profiles; including anxiolysis, anticonvulsion, myorelaxation, and sedation; because they have high affinity for the benzodiazepine binding site of GABA-A receptors. The total extract from *S. baicalensis* partially blocked suppression of locomotion as well as behavioral changes induced by electroshock stress.[51]

Harpagophytum procumbens (Devil's claw)

H. procumbens DC (Pedaliaceae) is widely used in South African traditional medicine. Aqueous root extract of *H. procumbens* possesses anticonvulsant activity in the experimental animal model used. The effectiveness of the plant's extract in the experimental convulsion paradigm used probably suggests that the herb could be used in both *petit* and *grand mal* types of epilepsy. The plant's extract appears to be relatively more effective in PTZ- and PCT-induced convulsions.[52]

Delphinium denudatum (Jadwar)

D. denudatum Wall. (Ranunculaceae) is an indigenous medicinal herb popularly known as 'Jadwar' by the traditional healers. It is used for the treatment of epilepsy. Aqueous fraction (AF) exhibited dose-dependent activity against hind limb tonic extension phase (HLTE) of maximal electroshock (MEST) and comparatively stronger anticonvulsant activity against seizures induced by PTZ and BIC.[10]

Withania somnifera (Ashwagandha)

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.[2]

Leonotis leonurus (lion's tail)

Water extract of *L. leonurus* was tested for anticonvulsant activity against seizures produced in mice by PTZ, 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 PTZ (90 mg/kg)-induced tonic seizures.[53]

Magnolia grandiflora (Him-champa)

The ethyl ether (EE) and hydroalcoholic extract (HE) of *Magnolia grandiflora* L. (Magnoliaceae) seeds orally administered in a single dose of 250 and 200 mg/kg, exhibited abolition of the extensor reflex of maximal electric induced seizure test in 50 and 40% of the experimental animals, respectively. They significantly prolonged the sleeping time induced by pentobarbital [Table 2].[54]

Marketed formulations available in India

A variety of Ayurvedic medicines for epilepsy available in the Indian market include [Table 3].[55]

Common side effects occur with these herbal drugs, when taken in high doses are diarrhoea, indigestion, gastric irritation. (http//ayurmedinfo.com/2012/02/25 downloaded on 24/08/2013).

CONCLUSION

Anticonvulsant drugs of first generation-PB, PRD, PHT, CBZ and VPA–have an increased potential for interactions and side effects due to enzyme induction and/or inhibition. Second generation anticonvulsants Improved tolerability, pharmacokinetics and management, coupled with

Table 2: Plants used in the treatment of Epilepsy

Plant	Part used	Uses
Vitex agnus-castus	Fruit, leaves	Epilepsy, psychoactive
Casimiroa edulis (Rutaceae)	Leaves	Sedative, antiepileptic
Cestrum nocturnum (Solanaceae)	Leaves	Antiepileptic
Viscum capense (Loranthaceae)	Stem	Antiepileptic, asthma, irregular mensturation
Calliandra portoricensis (Mimosaceae)	Roots and stem	Gastrointestinal tract (GIT) problems and convulsions
Nigella sativa (Ranunculaceae)	Seed extract	Analgesic and central nervous system (CNS) depressant, antibacterial, antihistaminic, petit, mal epilepsy
Pimpinella anisum (Umbelliferae)	Essential oil from fruits	Anticonvulsant activity, muscle relaxant, hypothermic
Casimiroa edulis (Rutaceae)	Leaves	Sedative, anticonvulsant
Acorus calamus (Araceae)	Rhizome	Insomnia, melancholia, neurosis, epilepsy, antioxidant activity, antistressor activity
Hibiscus rosa-sinensis (Malvaceae)	Fresh flowers	Brain tonic, anticonvulsant, aphrodisiac
Lannea discolor (Anacardiaceae)	Leaves, stem-bark, roots	Convulsions and 'fits', diarrhea, abscesses and boils, infertility, menorrhagia
Rauvolfia caffra (Apocynaceae)	Stem-bark, root-bark, leaves	Mental problems, insomnia and hysteria, rashes, convulsions, asthma
Blumea alata (D. Don) DC. (Asteraceae)	Roots, leaves	Fevers, convulsions, constipation, colic and abdominal pains
Conyza scabrida DC. (Asteraceae)	Leaves, roots	Convulsions, colds and coughs, pleuritic pains
Vernonia neocorymbosa Hilliard (Asteraceae)	Leaves, twigs, root	Epilepsy, abortion, stomach ache, hysteria, irregular menstruation
Abrus precatorius L. (Leguminosae)	Leaves	Anticonvulsant
Kigelia africana (Lam.) Benth.(Bignoniaceae)	Fruits, stem-bark	Rheumatism, acne, pneumonia, convulsions, aphrodisia, hemorrhoids
Tecomaria capensis (Thunb.) Spach (Bignoniaceae)	Stem-bark, leaves	bacterial infections, stomach pains, influenza, pneumonia, convulsions
Boscia albitrunca (Capparaceae)	Roots, leaves, fruits	Hemorrhoids, inflamed eyes, epilepsy
Capparis tomentosa Lam. (Capparaceae)	Roots, leaves	Asthma, constipation, eye problems, convulsions
Maytenus senegalensis (Lam.) Celastraceae	Roots, leaves	Hemoptysis, respiratory ailments, epilepsy, body pains, constipation, diarrhea
Commelina Africana Linn. (Commelinaceae)	Roots	Insomnia, infertility, epileptic 'fits', heart complaints
Crassula alba Forssk. (Crassulaceae)	Leaves, twigs	Epilepsy, dysentery and diarrhea, bloody stools
Cucumis hirsutus Sond. (Cucurbitaceae)	Roots, fruits	Convulsions, abortion, penal, vulval sores
Euclea divinorum Hiern (Ebenaceae)	Fruits, roots, stem-bark	Convulsions, toothaches, constipation, schistosomiasis, chest pains
Croton gratissimus Burch. (Euphorbiaceae)	Stem-bark/roots/leaves	Edema (dropsy), coughs, inflammation, insomnia, aphrodisiac, epilepsy
Jatropha curcas Linn. (Euphorbiaceae)	Roots, seeds, leaves	Angina, herpes, malaria, jaundice, fevers, diarrhea, ringworm, rheumatism, convulsions

contd...

Table 2: Contd...

Plant	Part used	Uses
Abrus precatorius Linn. (Fabaceae)	Roots, leaves	Love and good luck charms, pleuritic chest complaints, eye ailments, contraception, convulsions
Acacia karroo Hayne (Fabaceae)	Stem-bark, leaves, gum	Colds, oral thrush, stomach ache, osteomyelitis, dizziness, convulsions
Mimosa pudica Linn. (Fabaceae)	Whole plant	Convulsions/epilepsy, dysmenorrhea, heart palpitations
Nuxia floribunda Benth. (Loganiaceae)	Leaves/stem-bark	Fevers, coughs, indigestion, influenza, infantile convulsions
Melia azedarach Linn. (Meliaceae)	Leaves, root-bark, heartwood	Abdominal pains, helmintiasis, epilepsy, fits/ convulsions, schistosomiasis, swollen legs
Phytolacca dodecandra L'Herit. (Phytolaccaceae)	Roots, leaves, berries	Urinary complaints, snakebite, epilepsy, uterine tumors
Oxygonum dregeanum Meisn. (Polygonaceae)	Roots, leaves	Abdominal pains, inflammatory conditions, schistosomiasis, convulsions, whooping cough
Rubus pinnatus Willd. (Rosaceae)	Roots, leaves	Toothaches, convulsions, chronic diarrhea, abdominal cramps, rheumatism
Catunaregam spinosa (Thunb.) (Rubiaceae)	Roots, leaves, fruits	Epilepsy and dizziness, fevers, aphrodisiac, headaches snakebite, nausea
Gardenia ternifolia Schumach. and Thonn (Rubiaceae)	Roots, leaves, twigs, fruits	Headaches, madness, coughs, asthma, dysmenorrhea, infertility, chorea, epilepsy and convulsions, earache, schistosomiasis
Clausena anisata (Willd.) Hook. F. ex Benth. (Rutaceae)	Roots, leaves, fruits	Convulsions, teniasis and other parasitic infections, constipation, rheumatism, malaria and fevers
Englerophytum magalismontanum Krause (Sapotaceae)	Roots, fruits	Epilepsy, headaches, abdominal pains
Datura stramonium Linn. (Solanaceae)	Leaves, fruits, aerial parts	Gout, boils, abscesses and wounds, aphrodisia, motion sickness, sore throat and tonsilitis, visceral pains, epilepsy and Parkinsonism
Clerodendrum glabrum E. Mey. (Verbenaceae)	Leaves, roots	Fevers, intestinal parasites, childhood convulsions, colds
Lippia javanica (Burm. F.) Sreng. (Verbenaceae)	Leaves, twigs	Coughs, colds, bronchitis, asthma and other chest ailments, malaria, fevers, stomach problems and headaches, convulsions, cataracts
Rhoicissus tridentata (Linn. F.) Wild and Drum. (Vitaceae)	Roots, tubers, leaves	Epilepsy, dysmenorrhea, safe delivery in pregnancy, renal complaints
Flacourtia indica Willd (Flacourtiaceae)	Sterm-barks, fruits, leaves	Epilepsy, headache, fever, stomach-ache, diarrhea sleep disorders
Jatropha gossypiifolia Linn. (Euphorbiaceae)	Leaves, roots	Convulsions, fever, hypertension, convulsions,
Senna singueana (Caesalpiniaceae)	Leaves, flowers, barks, roots	Fever, conjunctivitis, convulsions, gonorrhea, bilharzias, stomach-aches
Terminalia mollis Laws (Combretaceae)	Roots	Epilepsy
Trichilia emetic Vahl (Meliaceae)	Roots, barks	Epilepsy, anti-parasitic diseases, head aches
Vitelaria paradoxa (Sapotaceae)	Leaves, barks	Convulsions, epilepsy, headaches, stress, head aches
Tetrapleura tétraptera Taub (Mimosaceae)	Barks, fruits, roots	Epilepsy, convulsions, fevers, malaria

GIT: Gastrointestinal tract; CNS: Central nervous system

fewer interactions, improve compliance, increase the safety and effectiveness and, probably, lower teratogenicity.[25] Adverse effects of the antiepileptic treatment may affect the patient's quality of life to a greater extent than the occurrence of seizures, and here lies a trade-off for the treating physician, because highly efficient AEDs are often associated with adverse effects, and an AED can have serious adverse effects in total absence of efficiency.[56]

An alternative therapy should be employed for the treatment and control of epilepsy due to the adverse events associated with the synthetic drugs. Ayurvedic treatment which are having lesser side effects in comparison to synthetic drugs can be an option for the control and treatment of epilepsy.

On the basis of the present review we are not in a position to provide a straightforward answer to the most pertinent question, i.e., whether AEDs in therapeutic doses have any cognitive effects at all, good or bad.[57]

The Ayurvedic literature contains treaties on epilepsy like symptoms, causes recognition, and treatment.

Table 3: Marketed formulation available in India

Product/dose	Manufacturer	Price (INR)	Formulation
Asvagandhadyarishta (20-40 ml)	Zandu Pharmaceuticals Works Ltd	80	Liquid
Bali tail	Sandu Pharmaceuticals Limited	-	Oil
Brahmi ghruta (12 mg)	Shree Baidynath Ayurved Pvt. Ltd	216	Tablet
Chandanadi tail	Arya Vaidya Pharmacy	414	Oil
Chaturmukha rasa (125-250 mg)	Dabur India Ltd.	77	Tablet
Haratala bhasma (1/4-1/2 ratti)	Divya Pharmacy	31.25	Powder
Kalyanaka ghruta (125 mg)	Nagarjuna Ayurvedic Group	71.90	Tablet
Kumaryasava (125 mg)	Dabur India Ltd.	82	Tablet
Mahakalayanaka ghruta (125 mg)	Nagarjuna Ayurvedic Group	98.95	Tablet
Mahamrutyunjaya rasa (125-250 mg)	Uma Ayurvedics Pvt Ltd.	98.95	Tablet
Rajata bhasma (1/2 ratti)	Divya Pharmacy	-	Powder
Saarasvatarishta (20-40 ml)	Uma Ayurvedics Pvt Ltd.	-	Tablet
Sarpagandha vati (125 mg)	Dabur India Ltd.	80	Powder
Svarna bhasma (1/8-1/4 ratti)	Shree Dhootapapeswar Ltd.	67.95	Liquid
Svarnamakshika bhasma (102 rtti)	Divya Pharmacy	1,030	Powder
Vaatakulantaka rasa (125-250 mg)	Dabur India Ltd.	78	Tablet
Yogendra rasa (125 mg)	Dabur India Ltd.	79	Tablet

INR: Indian rupee

Herbal and dietary therapies, which are recommended for external application, internal application, and topical use in the eyes and nose include bramhirasayan, bramhighritam, Ashwagandha, old pure desi ghee, daily fresh juice of Brahmi (*B. monniera* and *Centella asiatica*) with honey, and garlic juice in oil and powdered root of wild Asparagus (*Asparagus racemosus*) with milk.[7]

When compounded and prescribed appropriately, the safety of traditional herbal medications is high. It is generally recognized that life-threatening events are rare, compared to the hundreds of thousands reported for pharmaceutical products each year. This is due to the moderate bioreactivity that is imparted by most herbal preparations and the knowledge that is known regarding parameters of use.[58]

Indeed, preclinical work at Harvard and elsewhere based on this approach suggests that the study of herbal therapies and herbal-derived compounds may yield promising candidates for further clinical development. Herbal therapies may, therefore, potentially yield new treatment options for patients whose seizures are uncontrolled despite available AEDs, and may also represent inexpensive, culturally acceptable treatments for the millions of people around the world with untreated epilepsy.[7]

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