

REVIEW ON EPILEPSY AND ITS SYNTHETIC AND HERBAL APPROACH

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ABSTRACT

Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological and social consequences of this condition. Epileptic seizures are the result of excessive and abnormal nerve cell activity in the cortex of the brain. In epilepsy, the resistance of excitatory neurons to fire during this period is decreased. The diagnosis of epilepsy is typically made based on observation of the seizure onset and the underlying cause. Antiepileptic drug (AED) treatment should never be started as a trial to 'test' the diagnosis; this

will only cause problems for the physician and the patient, and is generally unhelpful in resolving diagnostic uncertainty. AEDs are prescribed after a careful evaluation of the risks and benefits of treatment. *Acorus calamus* found to have many phytochemical constituents namely alpha-asarone, Beta-asarone and eugenol. It was found that alpha asarone modulates GABAergic transmission in hippocampus in experimental animal which exerts its antiepileptic action.

KEYWORDS: Acorus calamus, Epileptic seizures, Antiepileptic drug, neurobiologic.

INTRODUCTION

Epilepsy is a chronic disorder of the brain affecting the people worldwide. It is characterized by recurrent seizures, involving brief episodes of involuntary movement involving a part of the body (partial) or the entire body (generalized) and is sometimes accompanied by loss of consciousness and control of bowel or bladder function.

In 2005, a Task Force of the International League Against Epilepsy (ILAE) formulated conceptual definitions of “seizure” and “epilepsy”. (Robert S. Fisher 2014).

“An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.”

A seizure is the clinical manifestation of an abnormal, excessive, hypersynchronous discharge of a population of cortical neurons. Seizure episodes are a result of excessive electrical discharges in a group of brain cells. Such discharges can take place at different parts of the brain site. Seizures vary from the briefest lapses or muscle jerks to severe and prolonged convulsions. Seizures vary in frequency too, from less than 1 per year to several per day.

One seizure does not signify epilepsy (up to 10% of people worldwide have one seizure during their lifetime). Epilepsy is having two or more unprovoked seizures.

Epilepsy is a disorder of the central nervous system characterized by recurrent seizures unprovoked by an acute systemic or neurologic disturbance. Epileptogenesis is the sequence of events that turns a normal neuronal network into a hyperexcitable network.

Mechanism of Epilepsy

During the normal function, the brain must achieve an ongoing imbalance between excitation and inhibition, to remain responsive to the environment without continued unstrained spontaneous activity. The inhibitory transmitter gamma aminobutyric acid (GABA) is important, it acts on ion channels to enhance chloride inflow and reduce the chances of action potential formation. Excitatory amino acid (glutamate and aspartate) allows influx of sodium and calcium, which produces the opposite effect. (Brian R. Walker 2014).

The exact mechanism of epilepsy is not known, (Jeffrey Noebels 2012) but a little is known about its cellular and network mechanisms. However, it is unknown under which circumstances the brain activity shifts into the activity of a seizure with its excessive synchronization. (Michel Le Van Quyen 2003) Epileptic seizures typically occur due to excessive firing and synchronisation of neurons. This results in the interruption of normal

working of the parts of the brain involved, leading to the clinical symptoms and signs of the specific type of epilepsy.

Seizure can result from an imbalance between excitatory and inhibitory transmission. The demonstration of intracellular recording during seizures shows a paroxysmal depolarisation shift in neuronal membrane potential, predisposing to recurrent action potentials.

Seizures are associated with episodic high-frequency discharge of impulses by a group of neurons present in the brain (Rang 2011). During epilepsy, the resistance of excitatory neurons to fire during this period is decreased, due to changes in ion channels or inhibitory neurons not functioning properly. This then results in a specific area known as "seizure focus" from which seizures may develop. The other mechanism of epilepsy may result from the up-regulation of excitatory circuits or down-regulation of inhibitory circuits caused due to an injury to the brain. Epileptogenesis can cause the secondary epilepsies. Failure in the functioning of the blood–brain barrier may also be a mechanism as it would allow substances in the blood to enter the brain and cause seizure. (Janigro 2006).

Method of detection

The primary discharge site and the extent of its spread is responsible for the determination of the symptoms that are produced, which range from a brief lapse of attention to a full convulsive fit lasting for several minutes, as well as odd behaviours. The particular symptoms produced depend on the function of the region of the brain that is affected.

Thus, involvement of the motor cortex causes convulsions, when hypothalamus is involved it cause peripheral autonomic discharge, and involvement of the reticular formation in the upper brain stem results in loss of consciousness. Abnormal electrical activity can be detected by electroencephalography (EEG) recording from electrodes distributed over the surface of the scalp during or following a seizure. The types of seizure can be recognised on the basis of the nature and distribution of the abnormal electrical discharge.

Generally, excitation will naturally tend to spread throughout a network of interconnected neurons but normally the inhibitory mechanisms prevent it. If excitatory transmission is facilitated or inhibitory transmission is reduced then epileptogenesis can arise. Because it is difficult to carry out detailed studies on epileptic patients, many different animal models of epilepsy have been investigated (R.Sarkisian 2001). These include a variety of genetic strains

that show epilepsy-like characteristics (e.g. mice that convulse briefly in response to certain sounds, baboons that show photically induced seizures and beagles with an inherited abnormality that closely resembles human epilepsy).

Antiepileptic Medication

Antiepileptic drugs are used in the treatment of epilepsy as well as non-epileptic convulsive disorders. With optimal drug therapy, epilepsy can be controlled completely in about 75% of patients, but about 10% continue to have seizures at intervals of 1 month or less. There is therefore a need to improve the efficacy of therapy. Patients with epilepsy usually need to take drugs continuously for many years, so avoidance of side effects is particularly important. Nevertheless, some drugs that have considerable adverse effects are still quite widely used even though they are not drugs of choice for newly diagnosed patient. (Rang 2011).

Antiepileptic drugs aim to inhibit the abnormal neuronal discharge rather than to correct the underlying cause. Three main mechanisms of action appear to be important:

1. Enhancement of GABA action.
2. Inhibition of sodium channel function.
3. Inhibition of calcium channel function.

Synthetic antiepileptic

The most important consideration before starting antiepileptic medication is to be secure of the diagnosis of epilepsy based on the clinical history. Antiepileptic drug (AED) treatment should never be started as a trial to 'test' the diagnosis; this will only cause problems for the physician and the patient, and is generally unhelpful in resolving diagnostic uncertainty. AEDs are prescribed after a careful evaluation of the risks and benefits of treatment. The decision to start medication is a major one – treatment will be for many years, even lifelong, and future withdrawal will bring its own issues around recurrence risk and driving, for instance. Antiepileptic drug (AED) treatment should never be started as a trial to 'test' the diagnosis; this will only cause problems for the physician and the patient, and is generally unhelpful in resolving diagnostic uncertainty.

The antiepileptic medication aims to prevent seizures with minimal discomfort to the patient. All AEDs have the potential for side effects and some have significant interactions with other medication. Choice of AED depends on the extent of the seizure type(s) and epilepsy syndrome. (HAMANDI).

Carbamazepine (CBZ) is a first class antiepileptic drug. Carbamazepine is voltage-gated sodium channels blocker. It acts by ionising within intracellular fluid, and is then binds to activated voltage-gated sodium channels, and thus prevents repetitive and sustained firing of an action potential. Leaving the affected cells less excitable until the drug dissociates. Carbamazepine is also a GABA receptor agonist, as it potentiates GABA receptors made up of alpha1, beta2, and gamma 2 subunits. CBZ is a first-line treatment for partial epilepsy, but is ineffective against absence and myoclonic seizures.

CBZ have an increased potential for interactions and side effects due to enzyme induction and/or inhibition. Common adverse effects may include drowsiness, dizziness, headaches and migraines, motor coordination impairment, nausea, vomiting, and/or constipation.

Herbal antiepileptic medication

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 has lesser side effects in comparison to synthetic drugs (Pandey Shashi Kr 2014). *Acorus calamus* (also called **sweet flag** or **calamus**) is a tall perennial wetland monocot of the Acoraceae family, in the genus *Acorus*. The rhizome of *Vacha* (*Acorus calamus*) has been used in Ayurvedic medicine for the treatment of various ailments, such as epilepsy, headache, eye disorders, insomnia, loss of memory, etc. Previous studies showed that *Vacha* rhizome is having significant anticonvulsant activity against various induced seizures models in experimental animals.

Acorus found to have many phytochemical constituents namely alpha-asarone, Beta-asarone and eugenol (Neumann 04 May 1989, Walter Simonetti 1990). It was found that alpha asarone modulates GABAergic transmission in hippocampus in experimental animal which exerts its antiepileptic action (Jing-Kun Miao 2013). Thus, *A. calamus* can emerge as new drug for epilepsy in near future by its antioxidant and modulation of GABA activity in central nervous system.

Present study has shown the anticonvulsant property of *A. calamus* in MES model of Swiss albino mice. The extract of *Acorus calamus* root was tested for its anticonvulsant activity, which showed that the extract significantly increased the latency period and reduced the duration of seizures induced by PTZ. Two mechanisms have been proposed for the mode of PTZ-induced convulsion either by inhibiting gamma amino butyric acid (GABA) pathway in

CNS (Corda MG 1990) or by increasing the central noradrenergic activity (W.P. De Potter 1980). The effect thus suggests its involvement in GABA-ergic or noradrenergic pathways and its efficacy.

CONCLUSION

Epilepsy is one of the most common neurological disorders with an incidence of 3% in the general population. Currently available Anti-epileptic drugs do not provide cure nor prevent relapse and they are often associated with serious side effects, including teratogenicity, chronic toxicity and adverse effects on cognition and behavior. This review clearly demonstrates the potency of Acorus plant.

Extract in successful treatment of epilepsy in different animal models. The phytoconstituents present in the extract have the promising effect in the management of epilepsy. This review gives a glance on the clinical effectiveness, minimal side effect profile and relatively low costs of herbal drugs in treatment and management of epilepsy compared to the synthetic drug CBZ. Further research should be done to isolate the bioactive components responsible for the antiepileptic activity in different types of seizures.

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