ejpmr, 2022,9(10), 257-264

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON ANTI CONVULSION HERBS IN SIDDHA MEDICINE

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Article Received on 15/08/2022 **Article Revised on 05/09/2022** **Article Accepted on 25/09/2022**

ABSTRACT

Epilepsy describes a condition in which a person has recurrent seizures due to a chronic, underlying process. It refers to a clinical phenomenon rather than a single disease entity, since there are many forms and causes of Epilepsy. The abnormal nerve impulse from cerebral nervous tissues may result in an almost instantaneous loss of consciousness, alteration of perception or impairment of psychic function, convulsive movements, disturbance of sensation or some combination of thereof. There are number of medicines are available for treatment of epilepsy in modern therapy. But the major disadvantage is their side effects. Treatment of epilepsy with herbal drugs is more beneficial with less side effects. There are number of drugs being used in the traditional siddha medicine for the treatment of epilepsy and some of them are scientifically ascertain their anti convulsing activity.

KEYWORDS: Anti Convulsion Herbs, Epilepsy in Siddha, Herbs for Epilepsy.

INTRODUCTION

Siddha system of medicine is the ancient, unique and potent system among all the system of medicine existing at present. It was invented by Siddhars who were spiritual scientist of the ancient Tamil land. Siddha science is a well defined science which was originated in the Lemurian continent, before the advent of any other medicine. It is a medical science through which the body as well as the soul are treated.[2]

According to Siddha system of medicine human body is made of seven basic physical constituents (*Udal thathukkal*) and the physiological function in the body is mediated by three humours such as *Vali, Azhal, Iyam* which are made up of five basic elements. Any derangement in these three humours and any variation in seven physical constituents leads to disease.

Epilepsy is known as *Valippu*. It is also known as *Isivu, Iluppu,* and *Vali*. In Siddha literature Epilepsy is classified into 21 types. Epilepsy occurs due to derangement of *Vatha Kaba* humor.[3] *Vatha* humour will be deranged by increased intake of biter, astringent and pungent taste foods, over eating, deep fried foods and the *kaba* humour will be deranged by emotional stress, increased sexual indulgence, and increased intake of cold foods. In epilepsy the deranged *Vatha Kaba* humour affects the *Abana vayu* and produces the disease.

Among the 70 million persons with epilepsy (PWE) worldwide, nearly 12 million PWE are expected to reside in India; which contributes to nearly one-sixth of the global burden. Epilepsy is the second most common and frequently encountered neurological condition that imposes heavy burden on individuals, families, and also on healthcare systems. As per a recent study, 70 million people have epilepsy worldwide and nearly 90% of them are found in developing regions.[4] Seizures can vary widely in their clinical presentation depending upon site, extent and mode of propagation of the paroxysmal discharge from the brain. Conventional medical treatments of epilepsy are not uniformly effective. A large number of agents called anti epileptic drugs are available to treat various types of seizures with the objective to reduce seizure frequency and the severity with the frame work of an acceptable level of side effects. Traditional herbs and compound medicines are useful for seizure management. Therefore alternative therapy including herbal and compound drugs is becoming increasingly popular.

Scientific validation of traditional medicinal plants for epilepsy

1. Butea monosperma

Butea monosperma is a moderate sized deciduous tree, belonging to fabaceae family. It is known as The Flame

of forest or Bastard teak in English and Palash or dhak in Hindi. They consists one of the largest families of flowering plants with 630 genera and 18000 species.[6]

The anti-convulsant activity of metholonic extract of leaves of Butea *monosperma* (100,200,400 mg/kg; p.o) was assessed by using Maximal Electroshock seizure (MES), Pentylenetetrazole (80 mg/kg; s.c) and Strychnine (4 mg/kg;i.m) induced seizures in mice. The extract significantly delayed the onset of convulsions induced by Pentylenetetrazole (PTZ) and Maximal Electroshock seizure (MES) in a dose dependent manner. Anticonvulsant effect of the extract was comparable to clinically used antiepileptic drugs (Diazepam). But, the extract did not protect the Strychnine induced seizure at significant level even in the dose of 400 mg/kg;p.o. These results suggest that the extract of *Butea monosperma* leaves possess anticonvulsant activity against Maximal Electroshock and Pentylenetetrazole induced seizure. The extract could have exhibited the activity by interfering with GABA, glutamatergic mechanism.[7] The anticonvulsive activity is due to the presence of a triterpene.[8]

2. Gmelina Arborea

Gambhari (Gmelina arborea Roxb.) belongs to the family Verbinaceae. It is found throughout greater part of India, Western Ghats, and from foot of North-West Himalaya to Chittagong & throughout Deccan Peninsula.[9] It is a medium sized to rarely large deciduous tree attaining a height of 15-20m.[10]

It is popularly known as Coomb teak, Cashmeri tree, Candhar tree in english.1 Kashmarya, Kashmeeri, Gambhari in Sanskrit. Different parts of the plant can be used medicinally like root, fruit, leaf, flower, bark.[11]

Gmelina arborea roxb is found in the tribal areas of Koraput district, Odisha, India. It is extensively used traditionally by the tribal people as anti helmintic, antimicrobial, anti-diabetic, hepato protective and anti-epileptic. The present study is an attempt to explore the anti epileptic activity of different fruit extracts of plant G.arborea using ethanol, ethyl acetate, n - butanol and petroleum ether as solvents. The extracts were screened for nontoxic properties examined by acute toxicity study and evaluated for their anti-epileptic activity. The anti epileptic activity of above extracts was evaluated by using strychnine induced tonic convulsion in Swiss albino mice. The extracts were found as nontoxic. All extracts were able to show antiepileptic activity at a single dose of 2 0 0 mg/ k g body weight (b.w.). The activities are comparable with the standard drug such as Diazepam. The dose of ethyl acetate, n - butanol and petroleum ether extracts of G .aborea showed lesser anti-epileptic activity than the standard drug diazepam except ethanol extract. Among all the solvent extracts, the ethanol extract showed better antiepileptic activity even in comparison with the standard drug. [12]

3. Pipper Nigrum & Pipper Longum

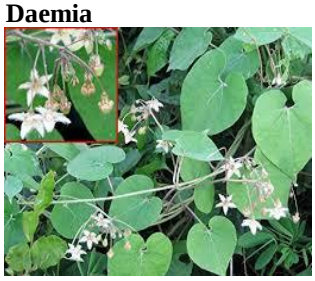
Piper nigrum (Piperaceae) is derived from piper, the Latin word for pepper. Most of the european names were derived from the Sanskrit, Pippali, a word used for this plant at least 3,000 years ago.[13]

Piperine is the main pungent alkaloid present in the fruits of black pepper (Piper nigrum) and long pepper (Piper longum) [14]. Black pepper is the most common culinary spice and considered an essential constituent of soups world-wide particularly in south Asia. In traditional medicine, black pepper has been used as an analgesic and anti-inflammatory agent and in the treatment of epilepsy and snake venom poisoning [15]. In Chinese herbal medicine, black pepper has a long tradition in the treatment of epilepsy.[16] The beneficial effects of black pepper in the management of pain and epilepsy may be attributed to its active constituent, piperine; however, its mechanism of action is still unclear. Piperine has been reported to have variety of pharmacological properties such as antipyretic, analgesic and anti-inflammatory.[17]

Piperine attenuated the PTZ and picrotoxin-induced seizures in mice. In the PTZ-induced seizures model, piperine and reference anticonvulsant drugs, carbamazapine, valproic acid and diazepam delayed the onset of seizures. Pentylenetetrazole (PTZ) has been reported to produce seizures by inhibiting gamma aminobutyric acid (GABA) neurotransmission [18]. GABA is the major inhibitory neurotransmitter substance in the brain, and is widely implicated in epilepsy. Enhancement of GABAergic neurotransmission has been shown to inhibit or attenuate seizures, while inhibition of GABAergic neurotransmission or activity is known to promote and facilitate seizures.[19-20]

Activation of GABA-ergic and/or opioid pathways contribute toward the observed analgesic and anticonvulsant effects of piperine.[21]

4. Pergularia Daemia



The plant Pergularia daemia (Asclepiadaceae) known as *"Veliparuthi*" in Tamil, "*Uttaravaruni"* in Sanskrit and *"Utranajutuka"* in Hindi. [22]

A slender, hispid, fetid- smelling perennial climber. Leaves opposite, membranous, 3-9 cm long and about as wide, broadly ovate, orbicular or deeply cordate, acute or short-acuminate at apex, pubescent beneath, petioles 2-9 cm long. A widely distributed in the tropical and sub tropical area. In India it is very commonly found in hedges through cut most of cenfry to an altitude about 1000m in Himalayas and 900m in Southern India.[23]

Pergularia daemia Forsk. (Choiv.) (Asclepiadaceae) is widely used in Cameroonian's folk medicine to treat epilepsy and infantile convulsions. In the present study, anticonvulsant effects of Pergularia daemia aqueous extract and possible antioxidant mechanisms were investigated on pentylenetetrazole (PTZ)-induced kindling model of epilepsy. Following the completion of behavioral studies, hippocampi were removed and oxidative stress parameters were determined. P. daemia extract (24.5-49 mg/kg) significantly protected mice against myoclonic jerks and clonic seizures. The extract (12.3-49 mg/kg) significantly decreased the number of myoclonic jerks and development of PTZ kindling. PTZ-kindling induced significant oxidative stress alterations that were reversed by the extract. These results suggest that P. daemia has anticonvulsant effects facilitated in part by antioxidant activities. This clarifies consequently, its use in traditional medicine to treat epilepsy in Cameroon. [24]

5. Nardostachys Grandiflora

Nardostachys jatamansi is a small, dwarf, hairy, perennial, rhizomatous, herbaceous, rare and most ancient species within family Valerianacae. Distributed in the Himalayas from Pakistan, in India including Jammu and Kashmir, Himachal Pradesh, Uttarakhand, Sikkim to Nepal. [25]

The anticonvulsant activity of ethanolic extract of nardostachys jatamansi roots was less when compared to Sodium Valproate in Maximal Electro Shock model. Whereas, in Pentylenetetrazole induced seizure model, anticonvulsant activity of ethanolic extract of nardostachys jatamansi roots was comparable to sodium valproate.[26]

By and large, the traditional system of medicine is slow acting as compared to the modern synthetic drugs because they are administered as crude preparations. A previous study has clearly shown that nardostachys jatamansi has an influence on the excitatory and inhibitory neurotransmission, of special interest being the increase in the gamma amino butyric acid (GABA) levels.[27]

6. Glycerrhiza Glabra

Glycyrrhiza glabra Linn. belongs to the family Leguminosae, is a genus of perennial herbs and under shrubs distributed in the subtropical and warm temperate regions of the world. Glycyrrhiza glabra Linn. commonly known as liquorice and sweet wood in english, Jothi madh, Mulethi in Hindi, Yashti madhuh, Madhuka in Sanskrit, Jashtimadhu, Jaishbomodhu in Bengali, Atimadhuranu, Yashtimadhukam in Telugu, Jethimadhu in Gujarati and Atimaduram in Tamil (Chopra et.al. 2002). Licorice extracts and its principle component, glycyrrhizin, have intensive use in foods, tobacco products and in traditional use and herbal medicine. [28]

The anticonvulsant activity of ethanolic extract of roots and rhizomes of *Glycyrrhiza glabra* (10, 30, 100 and 500 mg/kg, *i.p.*) in mice was assessed using maximum electroshock seizure (MES) test and pentylenetetrazol (PTZ) using albino mice. The lithium-pilocarpine model of status epilepticus was also used to assess the anticonvulsant activity in rats.

The ethanolic extract of *G. glabra* did not reduce the duration of tonic hind leg extension in the MES test even in the dose of 500 mg/kg. However, the extract significantly and dose-dependently delayed the onset of clonic convulsions induced by pentylenetetrazol. The dose of 100 mg/kg afforded protectionto all animals. The extract also protected rats against seizures induced by lithium-pilocarpine.[29]

7. Boerhavia Diffusa

Boerhaavia diffusa L. (Nyctaginaceae), commonly known as 'Punarnava' in the Indian system of medicine, is a perennial creeping herb found throughout the waste land of India. The roots are reputed to be diuretic and laxative and are given for the treatment of anasarca, ascites and jaundice. The *Boerhaavia* sp. has ancient medicinal use in different societies from the times of the B.C. The herbal medicine has evolved and changed through the years. A number of plant products have been identified through phyto-chemistry and the extract of their different plant parts are useful in various diseases without side effects. [30]

The study was carrired out to investigate the methanolic root extract of *B. diffusa* and its different fractions including liriodendrin-rich fraction for exploring the possible role of liriodendrin in its anti-convulsant activity. Air-dried roots of *B. diffusa* were extracted with methanol by cold maceration. The methanol soluble fraction of extract thus obtained was successively extracted to obtain liriodendrin rich fraction and two side fractions, that is, chloroform fraction and phenolic compound fraction. Anticonvulsant activity of methanolic extract and its different fractions, that is, liriodendrin-rich fraction and phenolic compound fraction were studied in pentyl enetetrazol (PTZ)-induced seizures.[31] Study showed the crude methanolic extract of *B. diffusa* and its liriodendrin-rich fraction showed a dose-dependent protection against PTZ-induced convulsions.[32]

8. Baccopa Monnieri

Bacopa monnieri (L), belonging to the Scrophulariaceae family and commonly known as Brahmi, is well known in India for its CNS activity but its neuropharmacological effect has not yet been explored. In the present study, the antiepileptic effects of the plant were investigated. The ethanolic extract of Bacopa monniera was tested for anticonvulsant activity in albino rats, using different convulsive models. The ethanolic extract of leaves produced significant anticonvulsant activity for all the different models studied. The present study shows a probable mechanism of action similar to that of benzodiazepines (GABA agonist). Thus, these results emphasize the need to diversify by using alternative therapeutic approaches pertaining to herbal medicine, where a single easily available plant may provide solutions to several therapeutic challenges, as observed in the anticonvulsant action of ethanolic extract of B. monniera.[33]

9. Pongamia Pinnata

Pongamia pinnata (L.) Pierre [family: Leguminosae] is a medium –sized glabrous tree popularly known as Karanja in Hindi, Indian beech in English and Pongam in Tamil. [34]

In the traditional system of medicines, such as Ayurveda and Unani, the Pongamia pinnata plant is used for anti-inflammatory, anti-plasmodial, antinonciceptive, anti-hyperglycamic, anti lipid peroxidative, anti-diarrhoeal, anti-ulcer, anti hyper ammonic and antioxidant activity (Chopade et al. 2009).

The present study was undertaken to investigate the anticonvulsant efficacy of the leaf extract of *Pongamia pinnata* using maximal electroshock-induced seizure (MES) in mice Freshly powdered leaves were evenly packed in soxhlet apparatus and extraction was done with 70% ethanol. The electric shock applied (150mA for 0.2s) through corneal electrodes to wistar albino mice produced convulsion and those showing response were divided into three groups of six animals. The group I treated with 1% normal saline (1 ml/100 gm, orally), Groups II treated with phenytoin sodium (25 mg/kg, i.p.) and Groups III treated with ethanolic extract of PPLE at a dose of (250 mg/kg i.p.). The ethanolic extract showed significant anticonvulsant activity by lowering the duration of extension phase (4.12±0.67) when compared to control group (9.64±0.41). These significant results indicate that the anticonvulsant action of *Pongamia pinnata* leaf extract on mice, probably due to the presence of flavonoids. [35]

10. Morringa Olirifera

Moringa oleifera is also known as horse radish tree and drum stick tree, belonging to family moringaceae and it is native to sub – himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. It is a small, fast growing, evergreen or deciduous tree. It usually grows up to 10 to 12 m in height. [36]

Moringa oleifera leaves extract restores mono amine levels of brain, which may be useful in Alzheimer's disease. *In-vitro* anticonvulsant activity from the aqueous extract of *Moringa oleifera* roots and ethanolic extract of leaves was studied on penicillin induced convulsion, locomotor behaviour, brain serotonin (5-HT), dopamine and nor epinephrine level and evaluated. [37]

11. Acorus Calamus

Acorus calamus L. commonly known as sweet flag belongs to the family of Araceae. It is perennial herb, which is indigenous to central Asia, India, and the Himalayan region, is found commonly on the banks of streams and in damp marshy places. It has a cylindrical rhizome with a diameter of 3 to 4 cm. The plant changes from pale green to pink as it grows. The leaf scars are spongy, brown and white in colour. The plant possesses slender roots, and its leaves are few and distichously alternate. [38]

A. calamus found to have many phytochemical constituents namely alpha-asarone, Beta-asarone and eugenol. [39-40] It was found that main constituent, alpha asarone modulates GABAergic transmission in hippocampus in experimental animal exerting its antiepileptic action. [41]

12. Zinziber Officicnale

Ginger, the rhizome of *Zingiber officinale*, is one of the commonly used species of the ginger family Zingiberaceae and is used for various foods and beverages.[42] Although probably a native of Asia, *Z. officinale* has become naturalized in many countries and is now widely distributed throughout tropical and subtropical parts of the world. Ginger has been cultivated for thousands of years for medicinal purposes and as a spice. It is used extensively in traditional medicine to treat cold, fever, headache, nausea, and digestive problems and is also used in western herbal medical practices for the treatment of arthritis, rheumatic disorders, and muscular discomfort.[43]

The main constituents of ginger are the gingerols, shogaols, paradols, and zingerone.[44] The major gingerol and shogaol components present in the rhizome of ginger are 6-gingerol and 6-shogaol, respectively. The main aroma defining component is zingiberol, whereas others such as gingediol, mono acyl digalactosyl -glycerol, di aryl heptanoids, and phyto sterols have also been identified.[45]

Plants and their phyto constituents have important role in the development of a potent anticonvulsant agent.[46]

The anti-convulsant activity can be due to the presence of various phyto constituents like phenyl propanoid, gingerol.[47] It has been suggested that MES induced convulsions are associated with oxidative damage.[48] *Zingiber officinale* also has strong antioxidant property (Kim *et al*., 2007). The anti-convulsant activity of *Zingiber officinale* rhizome can also be due to the antioxidant property.[49]

13. Ferula Asfotida

Plants of the genus *Ferula* belongs to the family of *Apiaceae* include about 130 species that distributed throughout central Asia and Mediterranean area.[50] *Ferula assa-foetida L*. is one of these species that grows wildly in central area of Iran. The part used of this plant and several other species of *Ferula* is an oleo gum resin (asafoetida) that obtained by incision of stem and root. This oleo gum resin is considered as an important matter of pharmacological and industrial application. The gum fraction of asafoetida contains the glucuronic acid, galactose, arabinose, and rhamnose and its resin is consisting of umbelliferone, ferulic acid and its esters, coumarins, sesquiterpene coumarins, and other terpenoids.[51] In Iranian folk medicine, asafoetida have been used for anti-convulsion, anti-spasmodic, carminative, digestive, expectorant, sedative, anti-

hysteric, laxative, aphrodisiac, anti-septic, and analgesic activities.[52] Recent pharmacological and biological studies have also shown several activities, such as anti-oxidant, anti-viral, anti-fungal, cancer chemopreventive, anti-diabetic, anti-spasmodic, hypotensive, and molluscicidal from this oleo gum resin.[51]

The anti-seizure profile of asafoetida may be related in part to monoterpens and terpenoid compounds present in the root because these compounds were also detected in *Ferula assa- foetida*.[53-54] It was determined that pinene analogs prevent idiopathic epilepsy in prone mice.[54] In addition, flavonoid compounds with anti-oxidant properties are among the fractions of *Ferula* plants and could be another candidate by which the anti-convulsant effect of *Ferula* is occurred. Phyto chemistry of asafoetida demonstrated that this oleo gum resin is the rich presence of alkaloids, flavonoids and acidic compounds. A large number of different sesquiterpene coumarins have been reported from asafoetida. The compounds of *Ferula assa-foetida* are not limited to sesquiterpene coumarins; it also contains some other compounds belonging to different classes of natural products, such as diterpenes phenolics, acetylenes, sesquiterpenes, and sulfur compounds.[55]

DISCUSSION

In Siddha texts, three basic factors have been implicated for the etiology of epilepsy. Endogenous factors (genetic, congenital, constitutional, enzymatic disturbances and idiopathic); Exogenous factors (intake of unwholesome and unhygienic foods, aggravation of Vatha humour due to trauma, worms and other environmental factors); and Psychological factors (excessive worry, grief, fear, passion, anger, anxiety and excitement). The aggravated humour spreads throughout the body through the nerves leading to the manifestation of the epileptic fit in the form of shaking jerks or convulsions or episodes of brief unconsciousness without shaking.

The herbs described in this article possess anti epileptic activity because most of these herbs contains GABA. GABA is the chief inhibitory neuro transmitter in the brain and it reduces the excitability of nerve cells in epilepsy. Most of the anti epileptic drugs available today have sedative action. They are physically and psychologically addictive. Withdrawal of the drug may be uncomfortable. On long term administration they also produce behavioural abnormalities. It is difficult to carry out the day to day activities in patients who are under anti epileptic treatment. Also many patients experience epileptic episodes even during the treatment course. So the above said herbs are chosen as a supportive drug in the treatment of epilepsy.

CONCLUSION

Living with epilepsy can be tough and cause the sufferer many problems. A person suffering from such a condition usually also gets attacks of depression, withdrawal from society, loss of health due to abnormal eating habits among other things. The herbs mentioned in this article are used by Siddha practitioners and from this review it is proved that these herbs have potent anti convulsion activity. So Modern and Ancient medicine systems should be combined to plan effective health-care delivery systems for better epilepsy care.

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