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Research Article

ANTICONVULSANT EFFECT OF CITHAREXYLUM QUADRANGULARE JACQ. LEAVES EXTRACTS IN STRYCHNINE INDUCED CONVULSION EPILEPSY MODEL IN SWISS ALBINO MICE

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ABSTRACT

Citharexylum quadrangulare (Jacq.), belonging to the family and commonly known as fiddle wood, in India. In the present study, the antiepileptic effects of the plant were investigated. The ethanolic extract and aqueous extract of Citharexylum quadrangulare (CQ) was tested for anticonvulsant activity. The present study shows probable mechanism of action similar to that of benzodiazepines (GABA agonist). Thus, these results emphasize the need to diversity 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 of ethanolic and aqueous extract of Citharexylum quadrangulare Jacq.

KEY WORDS: Anticonvulsant, Citharexylum quadrangulare, ethanolic and aqueous extracts, strychnine.

INTRODUCTION

Epilepsy is one of the frequently occurring neurological illnesses, characterized by recurring seizures with or without loss of consciousness, due to the abnormal discharge of cerebral neurons. It has a universal occurrence of 0.5-5% [1]. It is a chronic progressive disease and affects the quality of life [2]. The incidence of epilepsy in industrialized states is about 50 per 100,000 whereas, in emerging undeveloped states, it is 100 per 100,000 affecting individuals of all ages, races, and social groups [3]. Epilepsy has many possible causes such as infection, head trauma, brain malignancy and stroke. A variety of drugs including, antipsychotics antidepressants, levodopa, Thiazides diuretics and antibiotics, can also increase the frequency of seizures [4]. It is suggested that there is an imbalance between GABA and glutamate-mediated neurotransmission in the pathogenesis of epilepsy. Low catecholamine levels can be another causative factor of epilepsy [5, 6, 7]. The pathophysiology of the seizure disorder is complex. It may result from permanent modifications in the brain affecting neurotransmitters discharge and movement, receptors and ion channels, gene expressions, synapses and astrocytes. Initially, it was considered that modifications in

ion channels may cause the onset of the involuntary depolarization that begins seizures. Current researchers propose that numerous neuro chemical conduits contribute significantly to seizure onset and progression [8]. Epilepsy is not treatable but can be managed with anticonvulsant drugs which either prevent the initiation of convulsions or decrease the intensity of seizures [9]. Around, 70% of sufferers of epilepsy show better outcome on single drug therapy by currently available medicines. While 5-10% of patients are benefited by adding a second drug. Remaining 20 percent of patients are resistant to the treatment [10]. Therefore, there is need to develop a better anticonvulsant drug [11]. Anticonvulsant drugs of the first generation have a propensity for drug-drug interactions and side effects due to enzyme induction or inhibition [12]. Adverse effects of the antiepileptic drugs may affect the patient's quality of life to a greater extent than epilepsy itself which is a challenging situation for a physician [13]. Natural products are the potential basis of bioactive substances and are used worldwide as traditional medicinal remedies. Many of the synthetic drugs are derived from plant sources [14, 15]. Therapeutic plants identified to have anticonvulsant activity in animal models include *Abelmoschus angulosus, Allium sativum, Cinchona officinalis, Egletes viscosa, Cannabis sativa, Icacina trichantha, Magnolia grandiflora, Plumbago zeylanica, Artemisia spp, Bauhinia outimouta, Rauvolfia ligustrina and Ximenia Americana* [16]. Epilepsy is the 2nd greatest prevalent brain ailment after stroke and a huge load on the health system. Currently available antiepileptic drugs are associated with a lot of adverse effects and erratic pharmacological effects; hence it is crucial to explore newer anticonvulsant medications having better side effect profile and enhanced pharmacological effects as the treatment of epilepsy is for an extensive duration. Traditional herbal medicines are safer to use because of their moderate degree of bioreactivity. Researchers are trying to separate and distinguish the bioactive compounds of the medicinal plants which can be utilized in new drug development (22-25). *Citharexylum quadrangulare* Jacq. Is well identified old medicine plant belonging to the family Verbenaceae The study was executed consuming leaves *Citharexylum quadrangulare* J. A lovely small tree that offers interesting foliage all year round. Its large, oval, glossy leaves are green in winter, changing to shades of yellow, orange and gold for the months from spring to autumn. It bears small spikes of tiny flowers with a delicate scent in summer. Good for containers or tubs on the patio. [17]. The tree is harvested from the wild for local use as a food, medicine and source of a good quality wood. The wood is especially valued for making musical instruments, and the plant is often also grown as an ornamental [18, 19 and 20]. Citharexylum quadrangulare taxonomy Kingdom: Plantae, Subkingdom: Tracheobionta, Division: Magnoliophyta or Angiospermae, Class: Magnoliopsida, Subclass: Asteridae, Order: Lamiales, Family: Verbenaceae, Subfamily: Verbenoideae, Genus: *Citharexylum,* Species: *quadrangulare* Jacq., Binomial name: *Citharexylum quadrangulare.*

Citharexylum quadrangulare Jacq. Possess pharmacological activities like Antihyperlipidemic activity, Anti-inflammatory, Anticancer, Anti pyretic and analgesic, Dying agent, Antimicrobial and antidiabetic activity. The present study was especially designed to evaluate anticonvulsant effect Citharexylum quadrangulare Jacq. Leaves ethanol extract and aqueous extract in strychnine induced epilepsy model.

MATERIALS AND METHODS

Collection of plant

The whole plant, Citharexylum quadrangulare collected from Chalapathi Institute of pharmaceutical sciences in lam, Guntur. The plant was authenticated by Dr Satyanarayana head of the department of botany. Acharya Nagarjuna University.

Drugs

These include: strychnine (100mg/kg), phenytoin (30mg/kg), plant extract (150mg/kg).

Pharmacological activity

The method described by Porter et.al., (1984) was adopted in this study.

30 mice were divided into six groups each containing five mice.

Group-I → normal group/ control group (treated with saline water)

Group-II → standard group (treated with 30mg/kg phenytoin)

Group – III → test group (treated with plant extract 150mg/kg in tween-80 by oral route (ethanolic extract))

Group – IV → test group (treated with plant extract 150mg/kg in tween-80 by oral route (aqueous extract))

Based on the route of administration post-treatment, mice in all the groups received with 50mg/kg strychnine by the subcutaneous route.

RESULTS AND DISCUSSION

CQ at 150 mg/kg p.o caused a significant ($P<0.01$) delay in the onset of convulsion, 31.8 ±1.562 minutes. It shows very good protection compared to the control (Table I), whereas the phenytoin-treated group had 0% mortality and no convulsions. CQ significantly increased the onset time of the convulsion in this model. It is known that strychnine's lethal convulsant action is a result of glycine antagonism in the spinal cord. Thus, the probable mechanism may be Phenytoin -like, displacing strychnine from the receptor site (Nogardy, 1998). Thus, CQ may be clinically effective in seizures.

The duration of convulsions in Ethanolic and Aqueous extracts of Citharexylum quadrangulare leaves, groups which received extract at 150mg/kg body weight respectively and animals received standard drug phenytoin 3omg/kg body weight were reduced significantly decrease i.e., 3.6 ± 0.24, 4.8 ± 0.37, 6.4 ±0.5s respectively. The mortality rate in extracts groups which received 150mg/kg extract was 10% at 30 min and after 24 hrs in contrast animals which was 90%. Hence it revealed 100% protection in contrast to control animals. The graph represents the difference between control, standard, test-1 and test-2.

Table-01: Effect of Phenytoin, ECQ, and ACQ on Strychnine-induced seizures method

Treatment	Onset of convulsions (minutes)	Duration of convulsions (seconds)	Mortality
Control	4.2 ± 0.37	11.6 ±0.59	3/6
Standard	27.8 ± 0.86	6.4 ±0.5	0/6
Ethanolic	31.8 ±1.562	3.6 ± 0.24	0/6
Aqueous	31.2 ± 1.319	4.8 ± 0.37	0/6

Discussions

In the present investigation, anticonvulsant of Citharexylum quadrangulare. Jacq. of ethanolic and aqueous extracts evaluated in mice by strychnine induced convulsions at different extracts of administration. Phenytoin 30mg/kg was consumed as a standard drug. The time of onset of convulsions, duration of convulsions and mortality was recorded. Strychnine produces convulsions by interfering with the postsynaptic inhibition facilitated by glycine which is inhibitory neurotransmitter to the spinal cord neurons. Strychnine actions as a selective competitive antagonist to prevent the inhibitory actions of glycine act at the same receptors but varying positions. The levels of amino acid glutamic acid are also increased in brain, which acts as a neurotransmitter for exicitatory nerve impulses leading to myocontraction. (26). Administration of CQ in mice revealed significant delay in

onset of convulsions at 50mg/kg while highly significant delay 150mg/kg of ethanolic extract comparable to phenytoin. Frequency convulsions was also decreased highly ethanolic extract which were comparable to phenytoin duration of convulsions was decreased significantly at given dosage in comparison to control animals.

The observation of present study indicates that ethanol and aqueous extract Citharexylum quadrangulare possesses anticonvulsant activity in mice. GABA is the major inhibitory neurotransmitter in the brain while glutamic acid is an excitatory neurotransmitter in the brain. Seizures weaken the antioxidant defense mechanism of brain leading to free radical generation, which further provokes the oxidative stress and cause lipid per oxidation, brain edema and epilepsy. The inhibition of GABA neurotransmitter and the enhancement of the action of glutamic acid have been shown to be the underlying factors in epilepsy. The present study shows that the ethanolic and aqueous extract of Citharexylum quadrangulare leaves protected some of the animals against seizures induced by strychnine.

CONCLUSION

Present study gives several clues regarding the potential of Citharexylum quadrangulare Jacq. as anticonvulsant agent. Therefore, the results obtained from the study suggest that ethanolic extract of CQ has anticonvulsant property and the results verify its traditional use in epilepsy. Further phytochemical studies are in progress to isolate, characterize and identify the specific active compounds in this plant responsible for anticonvulsant activity.

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