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Anti – convulsant effect of ethanolic extract of *Ananyclus pyrethrum* root

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ABSTRACT

Anticonvulsant activity of the ethanolic extract of *Ananyclus pyrethrum* root was studied against maximal electro shock (MES) induced convulsions in mice. The extract suppressed hind limb tonic extensions (HLTE) induced by MES. In conclusion, the ethanolic extract of *Ananyclus pyrethrum* has anti convulsant effect in MES induced model which shows depressant action in the central nervous system.

Keywords: *Ananyclus Pyrethrum,* Anti-convulsant, MES Induced.

1. INTRODUCTION

Seizure is coined from the Latin word Sacire "To take possession of". Seizure (Convulsion) is therefore a paroxysmal event due to abnormal, excessive hyper-synchronous discharges from aggregates of central (Cerebral) neurons [1]. Even though, diversity of factors persuade the incidence and prevalence of seizures, in the region of 5%-10% of the population will have at least one seizure during their life time with the highest incidence occurring during early childhood and late adulthood and because seizure is common, this clinical condition is encountered frequently during medical practice in a variety of settings [1]. Seizures might occur in a variety of clinical settings, including febrile convulsion that is common in children, head injury, enclampsia in pregnancy, frank epilepsy, septicaemia, tetanus, meningitis, stroke, metabolic disorders and could be of different kinds [2]. Seizure in epilepsy is unprovoked, intractable and reoccurring unlike seizures in other settings that could be secondary [1, 3].

The majority epileptic patients do not only endure from stigmatization, they typically suffer from depression, muscular spasm, strange sensations, abnormal behavioural changes, convulsions, loss of consciousness and are highly prone to suicide and sudden, unexpected death[4]. Epilepsy affects natural intelligence among a studied group of Nigerian epileptics [5]. Recurrent excitatory activity or increased latency period of convulsion results in neurosis and dementia, as glutamate damages the brain cells [6]. Modern drug therapy tends to target certain strategies in the pathogenesis of seizure. The dentate gyrus (DG) is a gateway that regulates seizure activity in the hippocampus. Lamotrigine when used as an anticonvulsant, blocks both AMPA and NMDA receptors of glutamate [7]. During seizures, electrical impulses are distributed from one neuron in the brain to another through ion channels. Major ion channels include Sodium and Calcium. Therapeutic drugs in present use are therefore employed to block these ions thus proper the spread of seizure. Notable examples are phenytoin and carbamazepine that block Sodium ions and are thus used for grandmal seizures. Ethosuximide and valproic acid that block calcium ions in T-channel, are used for Petitmal seizures. A counter action of gamma amino butyric acid (GABA) which is inhibitory to the excitatory effect of glutamate/aspartate is employed in therapy. This includes the use of benzodiazepines or barbiturates as GABA-enhancers, gabatin, pregabalin and gabapentin as GABA analogues and vigabatrin or tiagabin as GABA hydrolysis inhibitors. Direct blockade of glutamate receptors is also employed in therapy. Lamotrigine acts in this manner [7]. These drugs/ strategies however bring about only symptomatic relief as they do not control epileptogenesis, the process by which the brain develops epilepsy [8,9].

Current research into antiseizure therapy is looking into the possibility of synthesizing drugs that can block the gliotransmission of ATP (adenosine tri-phosphate). This transmission in astrocyte-glia cells leads to astrocyte-calcium wave generation. Blockade of ATP signaling will not only decrease the frequency of epilepsy, it will make more adenosine available through further hydrolysis of ATP [8]. The list of anti seizures has even tripled in the 21 first centuries but, epilepsy remains a big clinical burden as no definite cure/control [9].More than one third of patients with epilepsy have inadequate control of seizures with drug therapy, as most drugs in current use are largely palliative and there currently exist no drug that has eliminated or prevented reoccurrence of epilepsy (Antiepileptogenic) [2]. An intriguing possibility is to control acquired epilepsy by preventing epileptogenesis, a process by which the brain becomes epileptic. A number of antiepiletics have been evaluated in clinical trials to test whether they prevent epileptogenesis in humans, but to date no drug has been shown to be effective in such trials. Thus, there is a pressing need for drugs that are truly antiepileptogenic to either prevent epilepsy or alter its natural course [9]. More than 80% of the world's population use or has at one time or the other used, or resorted to herbal remedy for treatment of ailments [10]. Medicinal plants have proven to be very good therapeutic agents just like the orthodox drugs but, unlike orthodox drugs, are said to exhibit only minimal or no side/ adverse effect [11].

Anacyclus pyrethrum (AP) is a perennial, procumbent herb, which is found throughout India. AP root contains essential oils and an alkaloid pellitorine that is intensely pungent constituent with a mixture of isobutyl amide. Traditionally, AP plant is used in traditional system of medicine and it is regarded as a tonic to the nervous system [12]. The antibacterial and anti-inflammatory activities are reported of the AP root [13,14]. *Anacyclus pyrethrum* is commonly known as 'Akarkara' in Ayurvedic texts, an indigenous medicinal plant widely used as medicine for promoting rejuvenation and vitality as a Vajikaran Rasayana [15]. Oral administration of the powder of this herb has been known to arouse sexual desire and improve ejaculatory time [16]. The plant *Anacyclus pyrethrum* has been reported as an effective remedy for the treatment of a variety of diseases. Apart from being designated as an aphrodisiac, *Anacyclus pyrethrum* is widely used in folk remedies for stimulating salivery glands and found useful in toothache, paralysis of the tongue and muscles of throat as well as neuralgic affections of the teeth [16]. *Anacyclus pyrethrum* root contains a colorless crystalline acid-amide known as pellitorine (pyrethrine). It possesses an intensily pungent taste and produces a sialogogue effect [17]. The other phytoconstituents reported in the plant include *N-iso*butyldienediynamide and polysaccharides[18, 19].

The objective of the investigation was to explore the potential effect of ethanolic extract of *Anacyclus pyrethrum* (A. pyrethrum) in mice as anti-convulsant agent.

2. MATERIALS AND METHODS

2.1. Plant material

The roots of *Anacyclus pyrethrum* were procured from ayurvedic drug store in Trivandrum, Kerala. The plant was authenticated by Botanist Dr. V. Chelladurai, Research officer-Botany (Retd.), Central council for research in Ayurveda and Siddha, Government of India.

2.2. Preparation of extracts

The roots of *A. pyrethrum* were powdered (500g) and ethanolic extract was prepared by simple maceration process using 2.5L of ethanol. The ethanolic extract was evaporated under reduced pressure using rotavapor evaporator. The yield of the extract was 1. 43% w/w. A suspension was prepared using 2% v/v tween 80 and administered orally.

2.3. Experiment Animals

The Institutional Animal Ethics Committee, (IAEC) approved the use of animals for the present study conducted at Arulmigu Kalasalingam College of pharmacy, Krishnankovil as per the requirements. Swiss albino mice weighing 18-25 g of either sex were used for the study.

2.4. Anticonvulsant activity

2.4.1. MES method

The anticonvulsant activity of extracts was evaluated for maximum electroshock induced seizure (MES) in mice. The electrical shock applied (150 mA for 0.2 s) through corneal electrodes to swiss albino mice produced convulsion and those showing response were divided into four groups of eight animals each. The first group of animals was administered normal tween 80 (5ml/kg) orally which served as negative control. II group of animals were treated with phenytoin sodium (25 mg/kg, i.p.) which served as positive control. III and IV groups of animals were treated with ethanolic extracts at different dose level. Drug pretreatment was given 30 min prior to the electric shock and animal were observed.

2.4.2. Statistical studies

Results were expressed as percentage (%) protection and mean ± SEM where applicable. Statistical significance was tested using student's t-test. The difference was taken to be statistically significant at *P<0.05*.

3. RESULTS AND DISCUSSION

MES was used to induce seizures and test drugs were administered to assess the effect on the seizures. The parameter assessed in animals was hind limb extension. When the mean hind leg extension of each group was compared with plain control, it was found that standard and extracts significantly reduced the duration of hind leg extension. When extract was compared with standard groups, no significant difference in mean scores was observed. The results are shown in table 1. In the present study we have evaluated the anticonvulsant activity of *Anacyclucs pyrethrum* using the MES models. EEAP (200mg/kg and 400mg/kg) has showed the decreased percentage of convulsions. It has often been stated that antiepileptic drugs that block MES-induced tonic extension act by blocking voltage dependent Na+ channels. In the present study EEAP does not showed significant results in MES model, so, our drug might not have inhibitory action on voltage dependent Na+ channels nor excitatory neurotransmitter mediated mechanism.

Table - 1: Anticonvulstant effect of ethanol extracts of *Ananyclus pyrethrum* by MES method

Treatment and dose (per Kg)	Reaction time (Sec) Mean ± SEM			
	Flexion	Extensor	Clonus	Stupor
Control Tween 80	19.66± 0.9888	31.73± 1.1524	17.10± 0.7231	67.16± 2.615
Phenytoin 25 mg/kg	10.58± 0.84**	16.46± 1.0312**	9.26± 0.978**	31.237± 0.0678**
Ethanol Extract 200 mg/kg	14.19± 0.49	21.52± 0.442*	17.67± 0.7491*	40.33± 1.979*
400 mg/kg	11.5± 0.61*	18.03± 0.2924*	12.92± 1.2352*	28.2± 1.5606*

P < 0.05 indicates the significant difference compared with control, * *= Highly Significant *= Significant.

4. CONCLUSION

In the present study, the ethanolic extract of *Anacyclus pyrethrum* was studied for anticonvulsant effect against MES model. *Anacyclus pyrethrum* at a dose of 400mg/kg has produced significant protective effect against PTZ model. The chemical constituent present in *Anacyclus pyrethrum* has to be explored to find the lead molecule which can be used for the treatment of petitmal type of epilepsy.

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