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ANTI CONVULSANT ACTIVITY OF *OCIMUM TENUIFLORUM* ON EXPERIMENTAL ANIMALS

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ABSTRACT

Epilepsy is defined as the repeated occurrence of sudden, excessive and/orsynchronous discharges in cerebral cortical neurons resulting in disruption of consciousness, disturbance of sensation, movements, impairment of mentalfunction, or some combination of these signs. The purpose of this investigation was to explore anticonvulsant activity of the leaf extract of *Ocimum tenuiflorum* using maximum electrical shock induced convulsion in rats. *Ocimum tenuiflorum* is an indegenious plant belonging to family Laminaceae, commonly known as krishna tulsi. Freshly powdered leaves were extracted with 70% ethanol. The convulsion is induced by electric shock to rats and those showing response were divided into four groups of six animals each. The group I treated with normal saline 1%, group II treated with Sodium valproate (90mg/kg), group III were treated with ethanolic extract of OTLE (100mg/kg) and group IV were treated with ethanolic extract of OTLE (200mg/kg). The ethanolic extract shows significant anticonvulsant activity by lowering the duration of extension phase (3.73 ± 0.59) when compared to control group (8.97 ± 0.47). From this research we concluded *Ocimum tenuiflorum* had significant anticonvulsant activity.

KEYWORDS: *Ocimum tenuiflorum*, Sodium valproate, OTLE, Convulsion, Intra peritoneal,

INTRODUCTION

Epilepsy is defined as the repeated occurrence of sudden, excessive and/orsynchronous discharges in cerebral cortical neurons resulting in disruption of consciousness, disturbance of sensation, movements, impairment of mentalfunction, or some combination of these signs. Seizures are called ictal events, from the latin ictus meaning "to strike".[1] In developed countries, annual new cases are between 40 and 70 per 100,000 people in the general population. This figure is often close to twice as high due to the higher risk of experiencing conditions that can lead to permanent brain damage. At the present day some of the antiepileptic drugs like Gabapentin, Lamotrigine, Tiagabine, Topiramate, Vigabatrin And Zonisamide, have been used for the treatment of epilepsy. They have all been shown to be effective in short-term addon clinical trials in patients with uncontrolled epilepsy. Synthetic antiepileptic drugs are associated with side-effects, including teratogenicity, chronic toxicity and adverse effects, on cognition and behavior.[2][3]

A seizure always is a symptom of abnormal function in the central nervous system (CNS) rather than a disease in itself.[4] A seizure discharge may be initiated in an entirely normal cerebral cortex by a variety of acute insults, such as withdrawal from alcohol, low blood sodium, or certain toxins. Seizures are to be distinguished from epilepsy, which is a chronic condition in which seizures occur repeatedly due to an underlying brain abnormality which persists between seizures.[5]

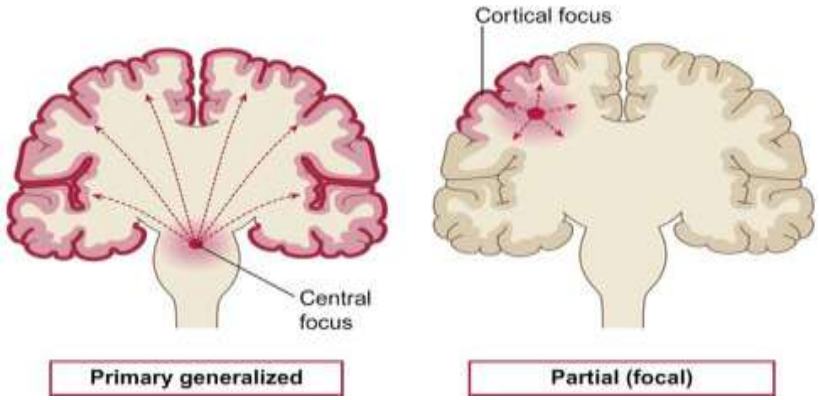

Fig No: 1 Abnormality with Seizures in different locations of brain.

Gamma-Aminobutyric acid (GABA), the main inhibitory neurotransmitter in the cerebral cortex, maintains the inhibitory tone that balances neuronal excitation. When this balance is perturbed, seizures may effect. GABA is formed within GAB Aergic axon terminals and released into the synapse, where it acts at one of two types of receptors, GABA-A, which

controls chloride entry into the cell, and GABA-B, which increases potassium conductance, decreases calcium entry and inhibits the presynaptic release of other transmitters.[6] GABA-A receptor binding influences the early portion of the GABA-mediated inhibitory postsynaptic potential, whereas GABA-B binding influences the late portion. GABA is rapidly removed by uptake into both glial and presynaptic nerve terminals and then catabolized by GABA transaminase. Experimental and clinical study evidence indicates that GABA has an important role in the mechanism and treatment of epilepsy.[7]

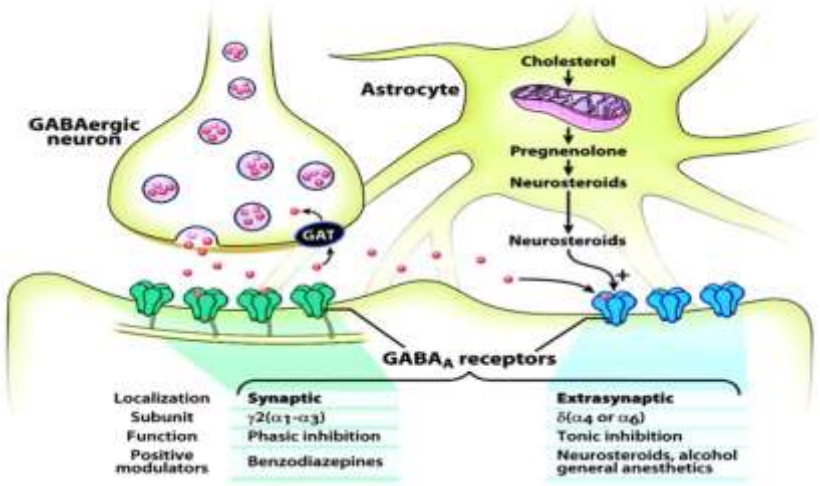

Fig No: 2 Mechanism of epilepsy on GABA receptors.

Epilepsy occurs in approximately 0.7% of the population at any one time. More than two-thirds of seizure problems begin in childhood, with a second peak of onset in the elderly. Usually, epilepsy does not significantly alter life expectancy, but quality of life may be seriously compromised when seizures are not satisfactorily managed.

Epilepsy is the chronic disorder of the central nervous system manifested by recurrent unprovoked seizures. Seizures are discrete; time limited alteration in brain function including changes in motor activity, autonomic function, consciousness, or sensation that results from an abnormal and excessive electrical discharge of a group of neurons within the brain. It has been shown to affect several brain activities and promote long-term changes in multiple neural systems. This disorder, if untreated, can lead to impaired intellectual function or death and is typically accompanied by Psychopathological consequences such as lose of self esteem.[8]

Medicinal uses of *Ocimum tenuiflorum*

Ocimum tenuiflorum fresh leaf juice is commonly used in cough, mild upper respiratory infections, bronchospasm, stress-related skin disorders and indigestion**.** It is combined with ginger and maricha (black pepper) in bronchial asthma. It is given with honey in bronchitis and cough. The leaf juice is taken internally and also applied directly on cutaneous lesions in ringworm. The essential oil has been used in ear infections.

The seeds are considered a general nutritious tonic. Pharmacological Action of *Ocimum tenuiflorum* is demulcent, expectorant, anticatarrhal, antispasmodic, anthelminthic. Other uses bronchospasm. *Ocimum tenuiflorum* have been recommended in various medical treatises for the cure of different diseases. *Ocimum tenuiflorum* belonging to the family, Laminaceae. It is a small evergreen tree, which is widely distributed in India. It has been recognized in different system of traditional medicines for the treatment of different diseases and aliments of human being. OTLE when applied on inflamed areas help to reduce pain and inflammation. It is beneficial to smear crushed leaves on skin rashes, ring worm affected areas and insect bites. Make a smooth paste of leaves and apply it on acne and pimple to see effective results. *Ocimum tenuiflorum* is very beneficial in fevers like dengue and malaria. Regular consumption of Ocimum leaves help to control diabetes and blood cholesterol.[9]

There is no information about anticonvulsant activity of *Ocimum tenuiflorum* in Experimental Animals Hence we have selected Ocimum tenuiflorum for studying its anticonvulsant effect on rat.[10]

Fig No: 3 *Ocimum tenuiflorum.*

MATERIALS AND METHODS

COLLECTION AND IDENTIFICATION OF PLANT

The fresh leaves of *Ocimum tenuiflorum* were collected in the month of January from Nellore, A.P, India and authenticated by Dr. C V S Baskar, MSc., PhD., Principal, VR College, Nellore.

PREPARATION OF OCIMUMM TENUIFLORUM LEAF EXTRACTS (OTLE)

Fresh leaves were collected and air dried in shade at room temperature. Dried leaves were powdered mechanically through mesh sieve. 100 g of freshly powdered leaves were evenly packed in soxhlet apparatus and the extraction was done with 70% ethanol. Then solvent was evaporated at low temperature under reduced pressure. In the preliminary phytochemical screening, the ethanolic extract of OTLE gave positive tests for glycosides, sterols, tannins and flavonoids. The residual extract was dissolved in sterile water and used for investigation.

PHARMACOLOGICAL STUDIES

Acute Oral Toxicity Study

Determination of LD50 value of *Ocimum tenuiflorum*

The procedure was followed by using OECD guidelines 423(Acute toxic class method). The acute toxic class method is a step wise procedure with 3 animals of single sex per step. Depending on mortality and / or morbident status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of test animals while allowing for acceptable data based scientific conclusion. The method uses defined doses (2000mg/kg) and the results allow a substance to be ranks and classified according to the globally harmonised system (GHS) for the classification of chemical which cause acute toxicity.[11]

Procedure

Twelve rats (Male wister albino rats, 150-200gm) were selected for studies. Starting dose level of ethanolic extract of *Ocimum tenuiflorum* was 2000 mg/kg body weight p.o. Most of the crude extract posses LD50 value more than 2000 mg/kg body weight of animal used.[12]

Observation

No toxicity or death was observed for these given doses, in selected and treated animals. So the LD50 of ethanolic extract of *Ocimum tenuiflorum* as per OECD guidelines-423 is greater than 2000 mg/kg. Hence the biological dose was fixed 100 mg/kg and 200 mg/kg for extract.

Evaluation of anticonvulsant activity

Animals

Male albino wister rats weighing about 150-250 gms were used in present study. All the rats were kept at room temperature of 22-25^{0}c in the animal house. All the animals were followed the internationally accepted ethical guidelines. Prior to the experiment rats were fed with standard food for one week in ordered to adapt laboratory conditions. All animal procedures were performed after approval from the institutional ethical committee and in accordance with the recommendations for proper care and use of laboratory animals.[13]

Chemicals

Sodium Valproate (Valpirin) manufactured by Cipla were purchased and preserved and used for further studies.

Instrument Used: Electro convulsive meter.

Experimental design

The anticonvulsant activity of *Ocimum tenuiflorum* leaf extract was evaluated for electric shock induced convulsions. The convulsions are induced by electric shock to albino rats. Rats those showing responses were divided into four groups of six animals each. The first group of animals were administered 1% normal saline as negative control. Group II animals were treated with sodium valproate (90mg/kg i.p) which served as positive control. Group III animals were treated with ethanolic extract of OTLE at a dose of 100mg/kg (i.p), Group IV treated with ethanolic extract of OTLE at a dose of 200mg/kg (i.p). Drug pretreatment was given prior to the inducing shock and each animal were placed in individual plastic cage and observed initially 30 min and later up to 24 hrs for the duration of flexion, extension and death recovery.[14]

Maximum Electric Shock Induced Seizures

The method used has been previously described by Two groups were treated with the extract, OTLE (100 and 200mg/kg *i.p*), one group was treated with sodium valproate (90 mg/kg, *i.p*) and the last group administered saline (25 ml/kg oral), to serve as control. After 30 minutes of drug treatment, tonic convulsions of the hind limb extremities of rat were induced by passing alternating electrical current (50 Hz, 60 mA and 0.2 s) through ear electrodes. This was the maximal current (60 mA) that induced tonic hind limb extension in all the trial mice and it was determined previously before commencement of the experiment. The number of animals

protected from tonic hind limb extension seizure and the time spent in this position were determined in each dose group.[15]

Statistical Analysis

Statistical analysis was done by one-way analysis of variance (ANOVA) followed by Student's t-test. Results are expressed as mean ±SEM from six rats in each group. P values `<0.001 were considered significant.

RESULTS

Ocimum tenuiflorum leaf extract was subjected for anticonvulsant effect using electric shock induced convulsion model in rats. OTLE exhibit significant anticonvulsant activity by lowering the duration of extension phase when compared to control group. The duration of tonic and hind limb extension in rats with 70% ethanolic extract was 3.73±0.59 at a dose 200mg/kg. The activity of ethanolic extract was comparable ($p<0.001$) to that produced by standard drug sodium valproate. Anticonvulsant activity of *Ocimum tenuiflorum* leaf extract on electrical shock induced convulsions in rats.

Table 1: Effect of extract in maximal electroshock seizures.

Treatment	Dose	Flexion	Extension	Convulsion	Recovery/death
Normal saline	1ml/100mg orally	3.81±0.35	**8.97±0.47**	4.62±0.69	Recovery
Sodium valproate	90mg/kg i.p	2.16±0.26	---	7.88±0.32	Recovery
Ethanolic extact	100mg/kg i.p	2.09±0.24	4.16±0.51	9.38±0.17	Recovery
Ethanolic extract	200mg/kg i.p	1.89±0.24	**3.73±0.59**	8.91±1.98	Recovery

DISCUSSION

There are a number of synthetic anticonvulsant drugs currently available for use in the management, control and treatment of individuals with epilepsy. However, most of the synthetic drugs are not only inaccessible and unaffordable, but also possess many toxic adverse effects. Therefore, there is a great need for the development of cheap, effective and safe anticonvulsant agents from plants and other sources.[16]

Protection against electric shock induced seizures in rats is used as an indication for compounds which may liable effective in grand mal epilepsy Electric stimuli evoke tonic hind limb extensions, which are suppressed by anti-epileptic drug. Varied mechanisms provide a broad spectrum of activity against seizures.[17] This is effective treatment of partial and primary generalised epilepsies. The tonic extensor phase is selectively abolished by the drugs effective in generalized tonic-clonic seizures. Phytochemicals such as quercetin, oils

are active principle responsible for anti-convulsant activity of *Ocimum tenuiflorum* is likely that flavonoid compounds, present in plants involved in this action. Hence this drug able to modulates the function of GABA of glutamate receptor.

CONCLUSION

The present investigation study was indicates that the plant *Ocimum tenuiflorum* has potential anticonvulsant activity against electrical shock induced convulsions in experimental animals. This activity of plant due to the compounds like quercetin, kaemferol, flavanoidal compounds and fixed oils. So *Ocimum tenuiflorum* uses for both ayurvedic and modern drug development areas because of its phytomedicinal uses.

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