Anticonvulsant Potential of Essential oil of *Artemisia abrotanum*

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Abstract
Epilepsy is a neurological disorder characterized by excessive electrical discharge in brain, which causes seizures. Epilepsy is the second most common neurological disorder in India. It is a very common disorder, characterized by seizures, which take various forms and result from episodic neuronal discharges, the form of the seizure depending on the part of the brain affected. The anti-convulsant properties of the essential oil obtained from the aerial parts of *Artemisia dracunculus* has been reported. The present study was aimed to evaluate the anticonvulsant potential of essential oil of *Artemisia abrotanum* which is available abundantly in Nilgiri Hills. The fresh leaves and flowering tops of *A. abrotanum* were subjected to extraction of essential oil by hydro distillation method using Clevenger apparatus. Experimental convulsion, in Swiss albino mice was induced by intra peritoneal administration of Pentylenetetrazole (PTZ) at 100 mg/kg in sterile distilled water after 1h administration of the test drug (100, 400 and 800 mg/kg). Then onset and latency of seizures and mortality were estimated and compared with the solvent control group. Diazepam (1 mg/kg), which was used as a positive control showed significant (P<0.01) delay in the onset of myoclonic seizures (49.0±1.95). However, at doses of 400 and 800mg/kg did not produce any significant changes in the convulsive parameters, when compared to control.

Introduction
Epilepsy is a neurological disorder characterized by excessive electrical discharge in brain, which causes seizures. Epilepsy is the second most common neurological disorder in India (1,2). Epilepsy affects an estimated 7 million people in India, and 50 million worldwide, approximately 40% of them are women. The prevalence of epilepsy is 0.7% in India, which is comparable to the Unites States and other developed nations. Epilepsy is a very common disorder, characterized by seizures, which take various forms and result from episodic neuronal discharges, the form of the seizure depending on the part of the brain affected. Often there is no recognizable cause, although it may develop after brain damage, such as trauma, infection or tumour growth, or other kinds of neurological disease, including various inherited neurological syndromes. Epilepsy is treated mainly with drugs, though brain surgery may be used for severe cases. Current antiepileptic drugs are effective in controlling seizures in about 70% of patients, but their use is often limited by side-effects (3).

Significant advances are being made in recent years to treat epilepsy using second-generation drugs. Polypharmacy is often advocated to 30%
of all epileptic patients for refractory partial or generalized tonic clonic seizures. However, none of the new drugs fulfills the ultimate goal of drug treatment of epilepsy, namely complete control of seizures (4).

A number of medicinal herbs containing Essential oils are reported to have Antiepileptic potential (5-10). The anti-convulsant properties of the essential oil obtained from the aerial parts of Artemisia dracunculus has been reported (11). Hence, the present study was aimed to evaluate the anticonvulsant potential of essential oil of Artemisia abrotanum which is available in Nilgiri Hills.

Materials and Methods

Aerial parts of Artemisia abrotanum was collected in the month of September 2005 from Medicinal Plants Development Area (MPDA), Doddabetta, The Nilgiris, identified and confirmed its authentification by comparing with voucher specimen by Dr. Suresh baburaj, Botanist, Survey of Medicinal Plants and collection Unit, Ooty.

Extraction

The fresh leaves and flowering tops were cleaned, cut into small pieces and subjected for extraction of essential oil by hydro distillation method using Clevenger apparatus. The distilled oil was collected and the residual water was removed by adding anhydrous sodium sulfate and stored in refrigerator.

Animals

Swiss albino mice (18-22 g) of female sex and male sex were used for acute toxicity and anticonvulsant studies, respectively. The animals were obtained from the Animal house, JSS College of Pharmacy, Ooty, maintained in suitable nutritional and environmental condition throughout the experiment period. The experimental protocol was approved by Institutional Animal Ethical Committee (IAEC) and CPCSEA to carryout pharmacological screening in animals (mice).

Acute toxicity studies

Toxicity study was conducted as per internationally accepted protocol drawn under OECD guidelines 423 in Albino mice (Swiss strain) at a starting dose level of 2000 mg/kg. Female mice (18-22g) were fasted for overnight and maintained with water ad libitum. The mice were separated into four groups of 5 in each. The essential oil was administered at a dose level of 2000 mg/ kg, orally as a solution in sesame oil and animals were observed individually and continuously for 30 min, 1, 4, 6, 12, 48 and 72hrs to detect changes in the behavioral responses like vocalization on touch, locomotor activity and palpebral reflex, and also autonomic responses like tremors, convulsion, salivation, diarrhea, sleep and coma and then monitored for any mortality for the following 14 days.

Screening of essential oils for anticonvulsant activity

Experimental convulsion, in Swiss albino mice was induced by intra peritoneal administration of Pentylenetetrazole (PTZ) at 100 mg/kg in sterile distilled water after 1h administration of the test drug. Then onset and latency of seizures and mortality were estimated and compared with the solvent control group. The standard drug, Diazepam (1 mg/kg) dissolved in sterile distilled water was used as positive control.

The male Swiss albino mice (18-22 g) were divided in to groups of 5 mice each. Group I received Sesame oil (1 ml/kg), served as solvent control. Group II received Diazepam (1mg/kg), served as Positive control. Group III, IV and V received essential oil of A. abrotanum at 100, 400 and 800 mg/kg respectively.

Statistical Analysis

The values are expressed as Mean±SE. The data were subjected to the One way Analysis of
Variance (ANOVA) followed by Dunnett’s multiple comparison test. The treatment groups were compared with the control group and P<0.05 was considered to be significant. Data analysis was carried out by using GrahPad Prism V.4

Results

GC analysis of the essential oil of *Artemisia abrotanum* have shown the presence of 19 compounds, which accounted for total 100% of oil. The presence of three compounds namely 1, 8-cineole, Davanone and Nerolidol at the retention time of 1.750, 14.717 and 10.883 min respectively have been confirmed by GC-MS analysis.

Diazepam (1 mg/kg), which was used as a positive control showed significant (P<0.01) delay in the onset of myoclonic seizures (140.3±19.78) and significant increase in time to death latency (1800±0.0) when compared to control. All the animals of the Diazepam group survived against the Pentylenetetrazole challenge.

The tested essential oil at 100 mg/kg showed significant (P<0.05) delay in the onset of myoclonic seizures (49.0±1.95). However, at doses of 400 and 800mg/kg did not produce any significant changes in the convulsive parameters, when compared to control.

Discussion

The most popular and widely used animal seizure models are the traditional MES and PTZ tests. Prevention of seizures induced by PTZ in laboratory animals is the most commonly used preliminary screening test for characterizing potential anticonvulsant drugs. The MES test is considered to be a predictor of likely therapeutic efficacy against generalized tonic-clonic seizures. By contrast, the PTZ test represents a valid model for human generalized myoclonic and also absence seizures. Other chemoconvulsant models for primary generalized seizures include bicuculine (α-amino butyric acid _α_ (GABA_α_) receptor antagonized), strychnine (glycine receptor antagonist) and aminophylline (adenosine-receptor antagonist). The PTZ (Metrazol) assay has been used primarily to evaluate antiepileptic drugs. However, it has been shown that, most anxiolytic agents are also able to prevent or antagonize Metrazol-induced convulsions. Generally, compounds with anticonvulsant activity in the petitmal epilepsy are effective in PTZ induced seizure model.

Lactones are common components in essential oils (specialy aromatic) bearing plants are extensively used in traditional medical systems in various parts of the world. Accordingly, essential oils have been revealing usual compounds as well as unexpected pharmacological activity. From the chemical and by/or ethno pharmacological point of view, the study of essential oils is further complicated by its rather complex mixture of compounds, the volatile nature of several commonly present constituents, the presence of photo reactive substances and the wide variability of the chemical profile obtained with different samples.

G.P.Coelho de Souza (1997) reported the presence of lactones viz., E-â-farnesene, â-decan-2-lactone, linalyl acetate and linalool in the essential oil of *Aeollanthus suaveolens* (used as an anticonvulsant in the Brazilian Amazon, has sedative properties). Our present study revealed the presence of linalool and â-farnesene in the essential oil of *Artemisia* species.

Some researchers have reported anticonvulsant activity of monoterpenes, SL-1, a synthetic monoterpene homologue of GABA, demonstrated anticonvulsant activity in PTZ induced seizures. Monoterpenes have protective effects against PTZ, picrotoxin and NMDA induced convulsions (15). The anticonvulsant activity of essential oil of *Lippia alba* (Verbenaceae) is also reported (16). Therefore it seems that antiseizure profile of *A.abrotanum* may be related in part to terpenoids present in the plant.
Mohammed Sayyah et al., (2004) (17) reported the anticonvulsant and chemical composition of essential oil of *Artemisia dracunculus* L. The GC-MS analysis showed that 68% of the essential oil was composed of monoterpenoids. Modulation of glutamatergic and GABAergic transmission mechanisms are indicated for anticonvulsant activity of the monoterpenes, trans-anethole, α and β-pinene and methyl eugenol (18, 19).

Hence, the monoterpenoids especially trans-anethole, pinene and methyl eugenol present in the essential oil of *A. dracunculus*, seems to mediate anticonvulsant activity. This is in agreement with the study of Sayyath et al., (2002) (20) where monoterpenes methyleugenol, eugenol and pinene present in the essential oil of *Laurus nobilis* (Lauraceae) protected mice against tonic convulsions induced by MES and PTZ.

GABA is the major inhibitory neurotransmitter in the brain and the inhibition of its neurotransmission has thought to be an underlying factor in epilepsy (21). The standard antiepileptic drugs, phenobarbitone and diazepam are thought to produce their antiepileptic effects by enhancing GABA neurotransmission (22).

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**References**

Table No:1 Anti convulsant activity of essential oil of *Artemisia abrotanum*

<table>
<thead>
<tr>
<th>Groups</th>
<th>Dose (mg/kg)</th>
<th>Onset of myoclonic seizure</th>
<th>Duration of clonic seizure</th>
<th>Latency to death</th>
<th>No. of animal survived</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10</td>
<td>39.75± 3.17</td>
<td>95.50± 24.60</td>
<td>427.4± 64.97</td>
<td>0/6</td>
</tr>
<tr>
<td>Diazepam</td>
<td>1</td>
<td>140.3± 19.78**</td>
<td>21.50± 4.48</td>
<td>1800.0± 0.0**</td>
<td>6/6</td>
</tr>
<tr>
<td>EOAA</td>
<td>100</td>
<td>49.0± 1.95*</td>
<td>42.0± 3.92</td>
<td>569.5± 75.87</td>
<td>3/6</td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>59.67± 5.60</td>
<td>50.0± 12.8</td>
<td>477.7± 63.78</td>
<td>1/6</td>
</tr>
<tr>
<td></td>
<td>800</td>
<td>56.0± 5.74</td>
<td>119.5± 29.77</td>
<td>882.3± 308.5</td>
<td>1/6</td>
</tr>
</tbody>
</table>

EOAA : Essential oil of *A. abrotanum*  
Superscripts ** and * statistical significance over control group at P< 0.01, P< 0.05.