INTRODUCTION

Epilepsy is a neurological disorder that affects a wide range of people throughout the world. It is the second most common chronic neurological condition seen by neurologists. Incidence of epilepsy in developed countries is approximately 50 per 100,000 while that of developing countries is 100 per 100,000[1]. India is home to about 10 million people with epilepsy [prevalence of about 1%][2]. The number of Epilepsy Specialists and Neurologists being very small in India, most people with epilepsy are being diagnosed and treated by non-specialists at both primary and secondary care levels. It is a disorder characterized by recurrent seizures of cerebral origin, presenting with episodes of sensory, motor or autonomic phenomenon with or without loss of consciousness[3]. It is a disorder of brain characterize by unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, synchronous and rhythmic firing of populations of brain neurons[4]. It has been observed that the presently available antiepileptic drugs are unable to control seizures effectively as in as many as 25% of the patients[5]. The conventional antiepileptic agents like phenytoin, carbamazepine and sodium sulphate carry with them several serious side effects notably neurotoxicity[6]. As majority of antiepileptic drugs are consumed life long, concomitant administration of other drugs predisposes to the risk of drug interaction. However, newer antiepileptics like gabapentin, vigabatrin, lamotrigine, etc are used supplemental to the conventional agents[4]. Thus, it is necessary to investigate for an antiepilepticagent that is highly efficacious as well as safe in terms of drug related toxicity.

Ethno-pharmacological research on natural products can contribute to the discovery of new, safe active compounds with novel structure that may serve as leads to the development of new antiepileptic drugs. Several plants of the families Euphorbiaceae, Leguminaceae, Labiatae, Liliaceae, Gentianaceae, Solanaceae, and Umbelliferae are used for the treatment of epilepsy in Indian traditional medicinal system [7]. The aim of treating anepileptic is not only to abolish the occurrence of seizures but also to lead a self sustained life. Melissa parviflora (MP) is pubescent or glabrate herb. The Muslim physician Behzad (1420-1515) in his book “Ilmul Advia” (Deva wears) and his colleague Khan al-Mahmud (1418-1495) in his book “Ilmul Advia F/O Medicine” in Unani division, Dr K. Krishnan Marg, New Delhi, India. Moreover the procured specimens were authenticated by a Taxonomist, Department of Botany, Jamia Hamdard. The plant MP (Unani name: Badranjboya) was purchased from Shamsi Dowakhana, Ballimaran, Delhi, India. The authenticity and identity was confirmed on the basis of classical description in Unani literature at Department of Ilmul Advia F/O Medicine (Unani), Jamia Hamdard, New Delhi and modern botanical information was established by matching with the specimens available at the National Institute of Science Communications. The wealth of Indian traditions, Dr K. Krishnan Marg, New Delhi, India. Moreover the procured specimens were authenticated by a Taxonomist, Department of Botany, Jamia Hamdard. The whole plant was collected, cleaned from debris and dried at room temperature. After complete drying, 200g of the powdered whole plant drug was used to prepare extract. 20g of the powdered whole plant drug was used to prepare extract. The extracts were conducted as per the procedures described from the extract were conducted as per the procedures described by Kokate presence flavonoids, saponins, carbohydrates, phenolic compounds and alkaloids.

Drugs

PTZ and Diazepam were purchased from Sigma Chemical Co. (Delhi, India). Different concentrations of the drugs were prepared freshly.
Acute toxicity study

Acute toxicity study was performed according to the OECD guidelines on Swiss Albino Mice and the animal were kept fasting for overnight providing water ad libitum, after which the extracts were administered orally up to 2000mg/kg b.wt and observed the mortality of animals.

Maximum electroshock induced seizure model

Electroconvulsive shock (50 mA for 0.2 sec) was delivered through ear electrodes to induce hind limb tonic extensions (HLTE) in mice. The extract was administered orally at the doses of 100 and 200mg/kgb.wt into test groups. Gum acacia in water and Diazepam (4mg/kgb.wt) were administered orally into two groups of animals as control and positive control groups, respectively. Electroconvulsive shock was delivered 60 min after the administration of drugs. Occurrence of HLTE and duration of seizures were noted closely for 2 min. The animals that did not exhibit HLTE were considered protected. Percentage of inhibition of seizures relative to controls was calculated[16].

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Dose mg/kg (p/o)</th>
<th>Onset time (Sec)</th>
<th>Duration of HLTE (Sec)</th>
<th>Percentage inhibition of convulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Group-I)</td>
<td>1 ml/kg</td>
<td>2.16±0.48</td>
<td>109.5±2.63</td>
<td>-</td>
</tr>
<tr>
<td>Diazepam (Group-II)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>MEP (Group-III)</td>
<td>100</td>
<td>6.67±0.49*</td>
<td>63.1±1.6*</td>
<td>42.3</td>
</tr>
<tr>
<td>MEP (Group-IV)</td>
<td>200</td>
<td>11.09±0.86*</td>
<td>30.46±4.04*</td>
<td>68.57</td>
</tr>
</tbody>
</table>

Values are given as mean ± SEM for six mice in each group. Results are statistically significant *P<0.001 as compared with control.

Table 2: Effect of Methanolic extract of Melissa parviflora on Pentylentetrazole induced Seizures in mice.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Dose mg/kg (p/o)</th>
<th>Onset time (Sec)</th>
<th>Duration of HLTE (Sec)</th>
<th>Percentage inhibition of convulsions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Group-I)</td>
<td>1 ml/kg</td>
<td>61.33±2.23</td>
<td>46.16±3.02</td>
<td>-</td>
</tr>
<tr>
<td>Diazepam (Group-II)</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>MEP (Group-III)</td>
<td>100</td>
<td>83.33±2.01*</td>
<td>31.33±1.73*</td>
<td>31.89</td>
</tr>
<tr>
<td>MEP (Group-IV)</td>
<td>200</td>
<td>95±1.67*</td>
<td>19±1.53*</td>
<td>58.84</td>
</tr>
</tbody>
</table>

Values are given as mean ± SEM for six mice in each group. Results are statistically significant *P<0.001 as compared with control.

DISCUSSION

Data from this study shows that MP significantly increases the onset time and decreases the duration of seizures by electroconvulsive shock. The study also revealed that the onset of tonic convulsion produced by PTZ was significantly delayed and also duration of seizures was prolonged. MES and PTZ may be exerting their convulsant effects by inhibiting the activity of gamma amino butyric acid (GABA) at GABA-A receptors [17]. PTZ produces jerky type of clonic convulsions in mice analogous to petit mal type of convulsions in humans[16]. A seizure reflects an imbalance between excitatory and inhibitory activity in the brain, with an increment of excitation over inhibition. Gamma amino butyric acid is the major inhibitory neurotransmitter which is implicated in epilepsy. The enhancement and inhibition of the neurotransmission of GABA will attenuate and enhance convulsion, respectively [19]. Diazepam a standard antiepileptic drug has been shown to exert their antiepileptic effects by enhancing GABA-mediated inhibition in the brain [20]. It is possible that Diazepam antagonize MES and PTZ convulsions in this study by enhancing GABA neurotransmission. The observations of our study indicate that the anticonvulsant effects of MP are possibly mediated by chloride channels of GABA/benzodiazepine receptor complex and by chloride channel of glycine receptor [Figure 1][21].

GABA plays a critical role in the etiopathology of epilepsy [22]. GAB Aergic mechanisms have been implicated in protection from a variety of chemo and electroshock induced seizures. Since the methanolic extract of MP delayed the occurrence of MES and PTZ...
convulsions, it is probable that it may be interfering with gabaergic mechanism(s) to exert their anticonvulsant effect. MP probably binds to a barbiturate-binding site of the benzodiazepine receptor to affect the duration of chloride channel opening, thereby influencing the epileptic seizures induced by MES and PTZ.

Phytochemical tests carried out in the present study show that the extract contains saponins, tannins and flavonoids. The plants containing saponins or flavonoids exhibit anticonvulsant activity[11, 12]. We may hypothesize that saponins and flavonoids present in MP might contribute to its CNS depressant and anticonvulsant activity. Further research is warranted in which the pure isolated components of MP may be individually evaluated for their CNS depressant and anticonvulsant activity to discover the exact mechanism accounting for its described activities.

Conflict of Interest

Authors do not have conflict of interest to present this work.

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