Depressant and Anticonvulsant Effect of Methanol Extract of *Swietenia Mahagoni* in Mice

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Abstract

The present study was undertaken to evaluate the sleep potentiation (depressant) and anticonvulsant effect of methanol extract from bark of *Swietenia mahagoni* L. Jacq. (MESM) (Meliaceae) in Swiss male albino mice. The sleep potentiation effect of MESM (25 and 50 mg/kg, i.p.) significantly increased pentobarbitone (45 mg/kg, i.p.) induced sleeping time in a dose dependent manner. The anticonvulsant effect of MESM at the doses of 25 and 50 mg/kg, i.p. was examined against pentylenetetrazole (PTZ, 80 mg/kg, i.p.) and strychnine (STR, 2.5 mg/kg, i.p.) induced seizures and significantly delayed (p < 0.05) the onset and also antagonized these seizures in a dose dependent manner. Diazepam (2.0 mg/kg, i.p.) was used as reference drug.

Keywords: Pentobarbitone, Anticonvulsant, Pentylenetetrazole, Strychnine, Swietenia mahagoni.

INTRODUCTION

Seizure is associated with disordered and rhythmic high frequency discharge of impulses by a group of neurons in the brain and status epilepticus is characterized by repeated episodes of epilepsy without the patient having recovered from the previous attack.¹

A large number of synthetic antiepileptic drugs are currently available to treat various types of seizures but unfortunately these drugs not only fail to control seizure activity in some patients, but they frequently cause side effects. Traditional medicine involves the use of herbal medicine, animal parts and minerals and about 80% of the world population is dependent (wholly or partially) on plant-based drugs.²

The *Swietenia mahagoni* L. Jacq. (Meliaceae) is a medium to large evergreen medicinally and economically important timber tree native to the West Indies and Central America and bark is grey-black in colour.³,⁴ The seeds and bark of this plant are used for the treatment of hypertension, diabetes and malaria as a folk medicine in Indonesia and India.⁴,⁵ The bark contains tannin, and may serve as an antipyretic, tonic and astringent.⁶ Traditionally the bark decoction of *S. mahagoni* is used to treat anemia, diarrhea, dysentery, fever, loss of appetite and toothache. The Leave decoction of *S. mahagoni* is used against nerve disorders, seeds infusion against chest pain and leaves or roots poultice against bleeding.⁷

The pentylenetetrazole (PTZ)-induced seizures are similar to the symptoms observed in the absence seizures and drugs useful in the treatment of absence seizures suppress PTZ-induced seizures.¹,⁸ The objective of the present study was to find out sleep potentiation effect of the methanol extract of *S. mahagoni* (MESM) on pentobarbitone-induced Swiss albino mice and also to investigate anticonvulsant activity against the seizures induced by PTZ and strychnine (STR).

MATERIALS AND METHODS

Plant material

The bark of *S. mahagoni* was collected in the month of October 2007 from the hill region of Midnapore, West Bengal, India. The bark was authenticated by M. S. Mondal, Botanical Survey of India, Kolkata, India and the voucher specimen (PMU-3/JU/2007) has been preserved in Pharmacology Research Laboratory, Jadavpur University, Kolkata for future reference.

Preparation of extract

The bark of *S. mahagoni* was shade dried and powdered with a mechanical grinder. The powder (750 g) was defatted with petroleum ether 60-80°C in a soxhlet extraction apparatus and then extracted with methanol.
The solvents were completely removed under reduced pressure to obtain a dry mass. The yields of the petroleum ether and methanol extracts were found to be 5.20 and 12.00% w/w respectively. The extracts were stored in a vacuum dessicator for further use. Preliminary phytochemical analysis showed that the triterpenoid and flavonoid are the major components of the extract.

**Animals used**
Male Swiss albino mice weighing (20-27g) were maintained in identical laboratory conditions and fed with commercial pellet diet (Hindustan Lever, Kolkata, India) and water *ad libitum*. All procedures described were reviewed and approved by the university animal ethical committee.

**Chemicals**
Pentobarbitone Sodium (Ranbaxy, Mumbai), Pentylenetetrazole (PTZ), Strychnine (STR) (HiMEDIA Laboratories Pvt. Ltd., Mumbai) and Diazepam were used for the study.

**Pentobarbitone-induced sleeping time in mice**
18-Male Swiss albino mice weighing 20-28 g were randomly divided into 3 groups (n=6). Group I received pentobarbitone sodium (45 mg/kg, *i.p*) and served as positive control. Group II and III received MESM (25 and 50 mg/kg, *i.p*) 30 min prior to the administration of pentobarbitone. The time between the loss of the righting reflex and the regain of this reflex measured as the sleeping time.

**Assessment of anticonvulsant activity**

**Pentylenetetrazol (PTZ)-induced seizure**
30-Male Swiss albino mice weighing 20-27g were randomly divided into 5 groups (n=6). Group I served as saline control (5 ml/kg, *i.p*). Group II received a convulsive dose of PTZ (80 mg/kg, *i.p*) and served as PTZ-control. Group III, IV and V received MESM (25 and 50 mg/kg, *i.p*) and reference drug diazepam (2.0 mg/kg, *i.p*) respectively, 30 min prior to the administration of PTZ. The animals were observed for onset of myoclonic spasm and clonic convulsion upto 30 min after PTZ injection. The percentages of protection were observed and recorded.

**Strychnine (STR)-induced seizure**
30-Male Swiss albino mice weighing 20-27g were randomly divided into 5 groups (n=6). Group I served as saline control. Group II received STR nitrate (2.5 mg/kg, *i.p*) and served as STR-control. Group III, IV and V received MESM (25 and 50 mg/kg, *i.p*) and reference drug diazepam (2.0 mg/kg, *i.p*) respectively, 30 min prior to the administration of STR. The animals were observed for onset of myoclonic spasm and clonic convulsion up to 30 min after STR injection. The percentages of protection were observed and recorded.

**Statistical Analysis**
All results are expressed as the mean ± SEM. The results were analyzed for statistical significance (*p*<0.05, *p*<0.01) by one-way (ANOVA) followed by Dunnett’s test using computerized Graph Pad InStat version 3.05, Graph pad software, U.S.A.

**RESULT**
The total sleeping time induced by pentobarbitone sodium increased significantly from 55.75 ± 2.17 min in the control group to 67.25 ± 2.56 and 96.25 ± 4.80 min in the extract treated group at the doses of 25 and 50 mg/kg respectively (Table 1).

PTZ and STR produced tonic seizures in all mice except saline control. The MESM (50 mg/kg) significantly delayed the onset of seizures from 1.64±0.24 to 5.4±1.28 min for PTZ (*p*<0.05) and 3.6±0.24 to 7.4±0.24 min for STR (*p*<0.01) induced seizures. The results of treated group are comparable with that of reference drug diazepam. (Table-2 and 3).

**DISCUSSION AND CONCLUSION**
Pentobarbitone sodium is a short to intermediate acting barbiturate, to produce quick onset of sleep. Pentobarbitone-induced sleep potentiation test has been used widely as an animal model in sleep studies and CNS depressant effects. In the present neuropharmacological screening it was observed that the methanolic extract of barks of *S. mahagoni* at the concentration 50 mg/kg prolonged the total sleeping time as compared to that of control group. This suggested that the MESM possess CNS depressant property.

Since many antiepileptic agents induce CNS depression, motor incoordination and ataxia, we therefore assessed the spectrum of anticonvulsant activity of MESM against PTZ and STR induced seizures. The PTZ test represents a valid model for human generalized myoclonic seizures and also generalized seizures of the petitmal (absence) type. STR is a potent spinal convulant and the convulsions produced by strychnine are reflex, tonic-
clonic and symmetrical. The MESM (50 mg/kg) significantly delayed (p<0.05) the onset and antagonized the PTZ and STR-induced seizures, which are comparable with the reference drug diazepam. Thus our present results suggested that the methanol extract of S. mahagoni may be effective against human generalized myoclonic seizures and also absence seizures.

Preliminary phytochemical analysis performed in this study showed that the triterpenoid and flavonoid are the major components of the extract. There are some evidences about anticonvulsant effect of some flavonoid compounds. Salgueiro et al., showed anxiolytic effects of some natural and synthetic flavonoids in rats and found that these compounds exerted their effects through the central benzodiazepine receptors. Some researchers have reported anticonvulsant activity of monoterpene. The SL-1, a synthetic monoterpene homologue of GABA, demonstrated anticonvulsant activity in PTZ-induced seizures. Therefore, it seems that the anticonvulsant effect of S. mahagoni may be related in part to flavonoid and/or triterpenoid compounds present in the extract.

It has been shown that PTZ enhances the basal activity and the sensitivity of dopaminergic neurons to PTZ in rat brain and the nigrostriatal dopaminergic neurons contribute to the central alterations associated with experimental epilepsy. The blockade of D₁ and D₂ receptors by haloperidol inhibited (-) bicuculline-induced seizures. Thus the blockade of DA receptor may have some protective effect in epilepsy.

The methanol extract of S. mahagoni was however more efficacious against PTZ induced seizure where protection was observed in all of the mice, an effect which indicates that the extract produce its central nervous system depressant action as consequence of its GABAergic and less importantly, glycineric transmission, since PTZ is a selective GABA₄ receptor antagonist while Strychnine antagonizes the inhibitory spinal cord and brainstem reflexes of glycine. From such informations it may be stated primarily that the methanol extract of bark of S. mahagoni may contain some biomolecule(s) that produce CNS depression and anticonvulsant action after blocking D₁ and D₂ receptors or facilitating GABA transmission.

In conclusion, the data of our study suggests that S. mahagoni may have beneficial effects in epilepsy that holds the hope of new generation of anticonvulsant drugs. However, comprehensive chemical and pharmacological research is required to find out the exact mechanism of this extract for its anticonvulsant effect and to identify the active constituent(s) responsible for this effect.

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Table 1: Effect of methanol extract of *Swietenia mahagoni* on pentobarbitone-induced sleeping time in mice (n=6).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Onset of sleep in minute (Mean±SEM)</th>
<th>Duration of sleep in minute (Mean±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pentobarbitone</td>
<td>45</td>
<td>2.5 ± 0.57</td>
<td>55.75 ± 2.17</td>
</tr>
<tr>
<td>II</td>
<td>Pentobarbitone+MESM</td>
<td>45+25</td>
<td>1.5 ± 0.57</td>
<td>67.25 ± 2.56</td>
</tr>
<tr>
<td>III</td>
<td>Pentobarbitone+MESM</td>
<td>45+50</td>
<td>1.5 ± 0.57</td>
<td>96.25 ± 4.80*</td>
</tr>
</tbody>
</table>

*P<0.01 when compared with control group; statistical analysis by Dunnett ’s vs. control.

Table 2: Effect of methanol extract of *Swietenia mahagoni* (MESM) on pentylenetetrazole (PTZ)-induced seizures (n=6).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Onset of sleep in minute (Mean±SEM)</th>
<th>Duration of sleep in minute (Mean±SEM)</th>
<th>Mortality (%)</th>
<th>Protection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Saline Control</td>
<td>5ml</td>
<td>0.0</td>
<td>0.0</td>
<td>100</td>
<td>0.0</td>
</tr>
<tr>
<td>II</td>
<td>PTZ</td>
<td>80</td>
<td>1.6±0.24</td>
<td>1.2±0.20</td>
<td>100</td>
<td>0.0</td>
</tr>
<tr>
<td>III</td>
<td>MESM</td>
<td>25</td>
<td>3.4±0.50</td>
<td>10±3.36*</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>IV</td>
<td>MESM</td>
<td>50</td>
<td>5.4±1.28*</td>
<td>9±1.18*</td>
<td>0.0</td>
<td>100</td>
</tr>
<tr>
<td>V</td>
<td>Diazepam</td>
<td>2.0</td>
<td>5.2±1.02**</td>
<td>10.2±1.02**</td>
<td>0.0</td>
<td>100</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01 when compared with control group; statistical analysis by Dunnett ’s vs. control.

Table 3: Effect of methanol extract of *Swietenia mahagoni* (MESM) on strychnine (STR)-induced seizures (n=6).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Onset of sleep in minute (Mean±SEM)</th>
<th>Duration of sleep in minute (Mean±SEM)</th>
<th>Mortality (%)</th>
<th>Protection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Saline Control</td>
<td>5ml</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>100</td>
</tr>
<tr>
<td>II</td>
<td>Strychnine</td>
<td>2.5</td>
<td>3.6 ± 0.24</td>
<td>11.6 ± 2.11</td>
<td>100</td>
<td>0.0</td>
</tr>
<tr>
<td>II</td>
<td>MESM</td>
<td>25</td>
<td>5 ± 0.54</td>
<td>11.8±1.96</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>V</td>
<td>MESM</td>
<td>50</td>
<td>7.4±0.24**</td>
<td>5.6±0.74*</td>
<td>0.0</td>
<td>100</td>
</tr>
<tr>
<td>V</td>
<td>Diazepam</td>
<td>2.0</td>
<td>7.6±0.67**</td>
<td>7.4±0.92</td>
<td>0.0</td>
<td>100</td>
</tr>
</tbody>
</table>

*P<0.05, **P<0.01 when compared with control group; statistical analysis by Dunnett ’s vs. control.
REFERENCES


