Evaluation of anticonvulsant and muscle relaxant activities of *Eclipta alba* using animal models

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**ABSTRACT**

*Eclipta alba* (L.) (*E. alba*) is commonly known as false daisy or bhringraj. It has great traditional importance because of being used as medicinal resource in India for centuries. It is reported to have anthelmintic, antipyretic, anti-inflammatory, antihistaminic, hepatoprotective, expectorant properties. Thus the present study has been undertaken to evaluate the anticonvulsant & muscle relaxant activity of *Eclipta alba* leaf extract (EALE) using animal models. *Eclipta alba* leaf extract (EALE) at doses of 50, 100, 200 and 400 mg/kg, p.o were studied for anticonvulsant and muscle relaxant activity on maximal electroshock-induced seizures (MES), rota rod and traction test respectively in rats. *Eclipta alba* leaf extract (200 and 400 mg/kg p.o.) reduced seizures induced by MES, decreased the duration of tonic hind limb extension (THLE) and decreased motor coordination showing anticonvulsant and muscle relaxant activity.

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INTRODUCTION

Eclipta alba (L.) (E. alba) is commonly known as false daisy or bhringraj. It is widely distributed throughout India, China, Thailand and belongs to the family Asteraceae [1]. The use of plant products for the treatment of human ailments has been a natural approach to health care since the beginning of civilization[2]. Herbs are supposed to be the source of many active substances which can be used therapeutically. Many medicinal herbs and spices find place in everyday use, many of these, are used for t/t of different diseases[3]. It is reported to have antihelmintic, antipyretic, anti-inflammatory, antihistaminic, hepatoprotective, expectorant properties [4,5] It has a great traditional importance because of being used as medicinal resource in India for centuries[6]. It is used as promoter of hair growth and blackener of hair[7] The leaf extract of E. alba is a powerful liver tonic and rejuvenative[8] The extract is also used as anti-venom against snake bites in China and Brazil [9] This plant has been used for the treatment of epilepsy in different cultures at different times,[10] Thus the present study has been undertaken to evaluate the anticonvulsant & muscle relaxant activity of Eclipta alba leaf extract(EALE) in rats employing maximal electroshock seizure models, rota rod and traction test .

MATERIALS & METHODS

Experimental animals –

Wistar albino rats of either sex weighing between 200-250 gms were purchased from OUAT, Bhubaneswar. Animals were housed maintaining 12:12 hr dark:light cycle. They had free access to standard chow diet & water ad libitum. Food but not water was withdrawn from rats 12 hours prior to the experiment. The animals were acclimatized to laboratory conditions one week prior to the experiments. The experiments were carried out during 10am to 4pm. All the experiments were conducted under isolated & noiseless conditions.

Drugs & Chemicals :

The drugs & chemicals for the entire research work, Diazepam & Phenytoin sodium were obtained in pure powdered form from the Ranbaxy Lab Ltd & Abbott laboratories, Mumbai respectively. Ethanolic extract of leaves of Eclipta alba (EALE) was procured from Envin Bioceuticals, Saharanpur, Uttarpradesh. Experimental protocol was approved by the institutional animals’ ethics committee before start of the study.

Experimental design :

Acute toxicity study -

OECD (Organization for Economic Co-operation and Development) Guideline was followed to study acute toxicity, fixed dose method; with starting dose of 2000mg/kg body weight was adopted. Starting dose of 2000mg/kg (per oral) of each was given to 5 animals (albino rats) & animals were kept for observation of behavioral change, death up to 72h [11].

Study of phytochemical constituents –

The dried leaves of eclipta alba have been reported to have coumestan derivatives like wedelolactone & demethylwedelolactone, desmethyl-wedelolactone-7–glucoside, unnamed alkaloid apigenin, luteolin, wedelic acid, ecliptin[12].

Evaluation of Anticonvulsant Activity -

Maximal electroshock seizure model (MES) :

MES seizures were evoked through transauricular electrodes with a current of 150 mA for duration of 0.2 s. The ethanolic extract of Eclipta alba was administered to a group of rats (n=6) in a dose of 50, 100, 200, 400 mg/kg, p.o, 1 h before application of electroshock. The duration of tonic hind limb extension was noted. [13] The percentage of protection was calculated. Phenytoin (25 mg/kg) was used as standard.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Drugs in mg/kg</th>
<th>Mode of administration</th>
<th>Nature of group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Distilled water-20</td>
<td>Through pediatric nasogastric tube</td>
<td>Control</td>
</tr>
<tr>
<td>2</td>
<td>Phenytoin-25</td>
<td>Dissolved in 1ml of distilled water</td>
<td>Standard</td>
</tr>
<tr>
<td>3</td>
<td>EALE-50</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>4</td>
<td>EALE-100</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>5</td>
<td>EALE-200</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>6</td>
<td>EALE-400</td>
<td>-do-</td>
<td>Test</td>
</tr>
</tbody>
</table>

Evaluation of Muscle Relaxant Activity:

Rota rod test:

The effect of EALE on motor co-ordination was assessed using Rota rod apparatus. The test was conducted on six groups of six rats each. Before giving the extract the rats were trained to remain on the rotating rod at the speed of 25 rpm for 5 min. The test compounds were administered intraperitoneally or orally. Thirty minutes after intraperitoneal or sixty minutes after oral administration the animals were placed for 1 min on the rotating rod. The number of animals falling from the roller 60 min. after the administration of ethanolic extracts (50, 100, 200 and 400 mg/kg) and 30 min. after the administration of diazepam (4mg/kg i.p.) were counted.[14]
**Traction test**

A 15 cm long twisted wire placed 20 cm above the table top was taken & forepaws of a rat was placed on it. Grasping the wire with forepaws and, placing at least one hind foot on the wire within 5 sec. when allowed to hang free was observed in normal rats. Failure to the traction was considered when the rats were unable to put up at least one hind foot on the wire. The test was conducted on six groups previously screened rats, one hour after giving the extract (50, 100, 200 and 400 mg/kg) and 30 min. after the injection of diazepam (4 mg/kg) [15]

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<tr>
<td>2</td>
<td>Diazepam (4mg/kg i.p.)</td>
<td>Dissolved in 1ml of distilled water</td>
<td>Standard</td>
</tr>
<tr>
<td>3</td>
<td>EALE-50</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>4</td>
<td>EALE-100</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>5</td>
<td>EALE-200</td>
<td>-do-</td>
<td>Test</td>
</tr>
<tr>
<td>6</td>
<td>EALE-400</td>
<td>-do-</td>
<td>Test</td>
</tr>
</tbody>
</table>

**Table 2:** Study protocol design for rotarod & traction tests in rats (approved by IAEC)

**Statistical analysis**

Statistical analysis was done by one-way ANOVA followed by Dunnett's multiple comparison test. \( P<0.05 \) was considered as significant.

**RESULTS**

**Anticonvulsant Assessment:**

*Effect of ethanolic extract of leaves of Eclipta alba on tonic hind limb extension in MES:*

The duration of tonic hind limb extension in rats treated with vehicle was 17.88±0.53 s. The ethanolic extract of leaves of *E.alba* showed a significant (\( P<0.01 \)) reduction in tonic extension phase (7.12±0.31 & 6.9±0.12 s) at a dose of 200 & 400 mg/kg respectively (Table 3)

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Group</th>
<th>Time of tonic hind limb extension in seconds (mean ± SEM)</th>
<th>% Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Distilled water(20mg/kg)</td>
<td>17.88 ± 0.53</td>
<td>91.25</td>
</tr>
<tr>
<td>2</td>
<td>Phenytoin(25mg/kg)</td>
<td>6.64±0.06*</td>
<td>91.25</td>
</tr>
<tr>
<td>3</td>
<td>EALE(50mg/kg)</td>
<td>12.39±1.28</td>
<td>38.47</td>
</tr>
<tr>
<td>4</td>
<td>EALE(100mg/kg)</td>
<td>10.80±0.32</td>
<td>49.23</td>
</tr>
<tr>
<td>5</td>
<td>EALE(200mg/kg)</td>
<td>7.12±0.31*</td>
<td>76.18</td>
</tr>
<tr>
<td>6</td>
<td>EALE(400mg/kg)</td>
<td>6.9±0.12*</td>
<td>89.84</td>
</tr>
</tbody>
</table>

\( P<0.01^{*} \), one-way ANOVA followed by Dunnett’s test

**Muscle Relaxant Assessment:**

The mean time spent on rotating rod was significantly decreased (\( P<0.001 \)) in animals treated with EALE as compared to control group, showing muscle relaxant activity and decreased motor coordination (Table 4)

<table>
<thead>
<tr>
<th>Dose(mg/kg)</th>
<th>Rotarod test</th>
<th>Traction test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fall off time</td>
<td>% decrease in performance</td>
</tr>
<tr>
<td>Control</td>
<td>280.31±6.79</td>
<td>0</td>
</tr>
<tr>
<td>Diazepam(4mg/kg)</td>
<td>18.93±0.12**</td>
<td>90.5</td>
</tr>
<tr>
<td>EALE(50mg/kg)</td>
<td>182.87±2.45</td>
<td>10.8</td>
</tr>
<tr>
<td>EALE(100mg/kg)</td>
<td>167±2.27</td>
<td>27.5</td>
</tr>
<tr>
<td>EALE(200mg/kg)</td>
<td>140.13±3.23</td>
<td>42.3</td>
</tr>
<tr>
<td>EALE(400mg/kg)</td>
<td>110.67±5.24*</td>
<td>65.4</td>
</tr>
</tbody>
</table>

All values are mean ± SEM,*\( P<0.01 \),**\( P<0.001 \) as compared to control group (Dunnet’s Test)
DISCUSSION

One of the frequently used animal models for evaluation of antiepileptic drugs is MES (maximal electroshock seizure) model. MES test describes the activity of different substances against generalized tonic clonic seizures. It also provides information regarding antiepileptic activity of substances against partial seizures. The present study showed the reduction in duration of THLE in MES models by the ethanolic extract of Eclipta alba revealing its anticonvulsant activity. The ethanolic extract of Eclipta alba at 400 mg/kg produced anticonvulsant activity in MES models indicating its beneficial effects in generalized tonic clonic seizure.

The study also proposes that the anticonvulsant dose produced muscle relaxant activity. A similar study showed high rutin present in Eclipta alba is responsible for its anticonvulsant activity.[16] Terpinoids, particularly triterpinoids and flavonoids derived from plants are reported to have muscle relaxant property[17] and anticonvulsant activity in various models for evaluation of antiepileptic activity like MES, PTZ, Picrotoxin etc.[18–22] The phytochemical screening of EALE also showed the presence of flavonoids and triterpenes. Therefore it may be concluded that the antiseizure and muscle relaxant activity of EALE is related to flavonoids and triterpenes present in extract.

CONCLUSION

The present study concludes that ethanolic extract of Eclipta alba leaves have significant anticonvulsant with muscle relaxant activity. But further studies are required to elucidate the complete and exact mechanism of action as well as the active ingredient producing these actions.

REFERENCES