Anticonvulsant action of aqueous extract of *Centella asiatica* and sodium valproate—A comparative study in pentylenetetrazole-induced seizures

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**ABSTRACT**

**Background:** Antiepileptics available currently cause teratogenicity and chronic toxicity. Several plant extracts exhibit the potential to be developed into newer antiepileptics. **Aims and Objective:** To evaluate the anticonvulsant action of aqueous extract of *Centella asiatica* and compare it with sodium valproate in pentylenetetrazole (PTZ)-induced seizures in albino mice. **Materials and Methods:** Twenty-four male albino mice weighing 18–30 g were divided into four groups. Group I was administered distilled water, group II sodium valproate (300 mg/kg i.p.), and groups III and IV aqueous extract of *C. asiatica* (100 mg/kg and 300 mg/kg), respectively. Seizures were induced by giving PTZ (80 mg/kg s.c.) 1 h after administration of the respective treatments. Suppression of clonic seizure was considered as an indicator of anticonvulsant action of the compound. **Result:** The aqueous extract of *C. asiatica* at both doses (100 mg/kg and 300 mg/kg) suppressed the clonic seizures in mice, and this was statistically significant. The anticonvulsant action of the extract at a dose of 300 mg/kg was comparable to that of sodium valproate in this study. **Conclusion:** The aqueous extract of *C. asiatica* at a dose of 300 mg/kg has shown anticonvulsant action comparable to sodium valproate in PTZ-induced seizures.

**KEY WORDS:** *Centella asiatica*; Pentylenetetrazole; Sodium Valproate

**INTRODUCTION**

Epilepsy is characterized by a group of disorders with recurrent episodes of seizures owing to a chronic underlying process. The lifetime risk of seizure is 5%, but highest risk is at extremes of age. More than 20% of the patients exhibit uncontrolled seizures in spite of availability of a number of antiepileptics. Current antiepileptics cause side effects such as teratogenicity, chronic toxicity, and adversely affect cognition and behavior. Hence, there is a need for development of new antiepileptics.

In traditional systems of medicine, *Centella asiatica* (Sanskrit—Brahmi) has been used for various skin diseases, leprosy, and malaria. It presents wound-healing and ulcer-healing properties, antinociceptive and anti-inflammatory properties, protective effect in psoriasis, cardioprotective property, immunomodulatory, cytotoxic, and antitumor properties, anxiolytic properties, and antioxidant and radioprotection properties. It is extensively used for epilepsy in Ayurveda. This study is done to evaluate the anticonvulsant action of *C. asiatica* and compare it with sodium valproate in mice.

**MATERIALS AND METHODS**

**Animals**

Male albino mice weighing 18–30 g were obtained from Central animal house, KIMS, Hubli. They were housed in standard laboratory conditions and had free access to food and water ad libitum. Food and water were withdrawn just before...
experimentation. They were divided into four groups, consisting of six animals each. The study protocol was approved by the institutional animal ethics committee.

**Drugs and Chemicals**
Sodium valproate (Sun Pharmaceuticals) and pentylentetrazol (PTZ) (HiMedia Laboratories) were used in this study. All drug solutions were freshly prepared in distilled water at room temperature.

**Plant Material**
*C. asiatica* plants were obtained from Ayurvedic Mahavidyalaya, Hubli. The identification of the plant was done by the head of the department of Rasayanashastra, Ayurvedic Mahavidyalaya, Hubli.

**Preparation of Aqueous Extract**
The aqueous extract was prepared by cold maceration method. The plants were air dried and powdered. Thirty grams of the dry powder was soaked in 200 mL of cold water at room temperature. The extract was filtered, and the filtrate was dried at room temperature in a steady air current.[24]

The test solution of *C. asiatica* was prepared by dissolving 2 g of aqueous extract in 100 mL of distilled water at room temperature. It had a concentration of 20 mg/mL.

**Preliminary Phytochemical Screening**
A preliminary phytochemical screening of the extract revealed that the major components are the triterpenes—asiatic acid and madecassic acid, and their derived triterpene ester glycosides, asiaticoside, madecassoside, and centelloside. It contains other components including volatile oils, flavonoids, tannins, phytosterols, amino acids, and sugars.[10,25]

**Assessment of Anticonvulsant Activity**

**PTZ-induced seizures**. The animals were divided into four groups (n = 6). Group I received distilled water orally, and it served as the control. Group II received 300 mg/kg of sodium valproate intraperitoneally, and it was the standard group.[26] Groups III and IV were the test groups that received 100 mg/kg and 300 mg/kg of aqueous extract of *C. asiatica*, respectively. After 1 h, PTZ (80 mg/kg) was administered subcutaneously. The duration of various phases of ensuing convulsions were noted and subsequent mortality recorded. The suppression of clonic seizure was taken as an indicator of anticonvulsant action.[27]

**Statistical Analysis**
The results were expressed as mean ± standard error of mean (mean ± SE). Results were analyzed by one-way ANOVA, followed by Bonferroni test as post hoc test. A p value less than 0.05 was considered significant.

**RESULT**
All animals in the control group (group I) developed seizures. All animals in standard group (group II) were protected by sodium valproate and did not develop seizures. Group III animals, which received 100 mg/kg of aqueous extract of *C. asiatica*, exhibited significant delay in the onset of seizures (p < 0.001) and suppression of clonic seizure (p < 0.01) when compared with control, and it was statistically significant [Table 1]. The aqueous extract of *C. asiatica* at a dose of 300 mg/kg (group IV) has exhibited complete suppression of seizures, and its anticonvulsant activity is comparable to sodium valproate [Table 1].

**DISCUSSION**
In this study, the anticonvulsant action of aqueous extract of *C. asiatica* was screened by PTZ method. The anticonvulsant action was compared with sodium valproate, which is considered as the standard drug for PTZ-induced seizures model. PTZ model is useful in screening of drugs effective in absence seizures.[27] In this study, the aqueous extract of *C. asiatica* at both doses (100 mg/kg and 300 mg/kg) has exhibited anticonvulsant action in the PTZ-induced seizure model. The anticonvulsant action of aqueous extract of *C. asiatica* at a dose of 300 mg/kg is comparable to

<table>
<thead>
<tr>
<th>Parameters (duration in seconds)</th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latency of seizure</td>
<td>330.66 ± 10.8</td>
<td>0</td>
<td>419 ± 8.73***</td>
<td>0</td>
</tr>
<tr>
<td>Tonic hind limb flexion</td>
<td>1.5 ± 0.23</td>
<td>0</td>
<td>1.5 ± 0.23NS</td>
<td>0</td>
</tr>
<tr>
<td>Tonic hind limb extension</td>
<td>10.66 ± 0.61</td>
<td>0</td>
<td>10.66 ± 0.43NS</td>
<td>0</td>
</tr>
<tr>
<td>Clonic seizure</td>
<td>5.5 ± 0.44</td>
<td>0</td>
<td>3.5 ± 0.44**</td>
<td>0</td>
</tr>
<tr>
<td>Postictal depression</td>
<td>340.16 ± 3.78</td>
<td>0</td>
<td>189.16 ± 1.15***</td>
<td>0</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SE.
n = 6, "p < 0.05, "p < 0.01, ""p < 0.001 (compared with control), NS, not significant.
sodium valproate. Hence, the aqueous extract of *C. asiatica* may play a role in the treatment of absence seizures. Many studies have reported the anticonvulsant action of *C. asiatica* in other models of epilepsy. In a study by Gupta et al,[28] the cognitive impairment and the oxidative stress induced by PTZ kindling was attenuated by *C. asiatica*. Katare and Ganachari[29] reported that *C. asiatica* has antilipidperoxidative and antiepileptic actions in the lithium-pilocarpine model of status epilepticus.

Visweswari et al,[30] found that one of the facets of anticonvulsant action of *C. asiatica* was by causing perceptible changes in the cholinergic system. In another study by Visweswari et al,[31] there was a decrease in Na⁺, K⁺-ATPase, Mg²⁺-ATPase, and Ca²⁺-ATPase activities in brain during PTZ-induced epilepsy. The levels of these ATPases were increased in brain by pretreatment with *C. asiatica* extracts except with aqueous extract. PTZ induces seizures by antagonizing the inhibitory gamma-aminobutyric acid (GABA)ergic neurotransmission.[32] Terpenoids, particularly triterpenoids and flavonoids, present in various plant extracts are reported to show anticonvulsant action in various epilepsy models such as PTZ model.[33] The phytochemical screening of aqueous extract of *C. asiatica* has revealed that it contains triterpenes and flavonoids. Hence, the anticonvulsant action of aqueous extract of *C. asiatica* is probably owing to the triterpines and flavonoids present in it. The mechanism of anticonvulsant action may involve cholinergic system, the GABAergic neurotransmission, and by modulation of ATPases (Na⁺, K⁺, Mg²⁺ and Ca²⁺) activities. However, there is a need for further studies to establish the exact mechanism of action.

**Table 2: Percentage protection from clonic seizures in PTZ method**

| Group I  | 0  |
| Group II | 100 |
| Group III| 0  |
| Group IV | 100 |

**CONCLUSION**

The aqueous extract of *C. asiatica* exhibits anticonvulsant action comparable to sodium valproate in PTZ-induced seizures. However, further studies are needed to elucidate the exact mechanism of anticonvulsant action of this extract.

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