Short communication

Anticonvulsant effect of Hypericum perforatum: role of nitric oxide

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Abstract

Hypericum perforatum L. is used in traditional medicine for its anticonvulsant property. We studied the anticonvulsant activity of the aqueous and ethanolic extracts of Hypericum perforatum aerial parts in mice in order to evaluate the traditional use of this plant. The pentylenetetrazole (PTZ) and the maximal electroshock seizure (MES) tests were used for assessing the anticonvulsive effects of this plant. In the PTZ test, the extracts (0.1–1 g/kg, i.p.) delayed the onset of tonic convulsions and protected mice against mortality. In the MES test, both extracts did not show an antiseizure activity. L-NAME (1–10 mg/kg, i.p.), a nitric oxide (NO) synthase inhibitor, reduced the anticonvulsant activity of the extracts. The results of this study indicate that the extracts of Hypericum perforatum aerial parts could contribute to the control of petit mal seizure and this effect may be partially mediated by nitric oxide pathway.

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Keywords: Hypericum perforatum; St. John’s wort; Anticonvulsant activity; Nitric oxide

1. Plant

Hypericum perforatum L. (Hypericaceae), aerial part collected from the suburbs of Binaloud (North of Iran) in July 2002, authenticated by Ferdowsi University (Joharchi), voucher samples were preserved at the herbarium of the Faculty of Pharmacy of Mashhad University of Medical Sciences [139-0816-1].

2. Uses in traditional medicine

A remedy for headache, paralysis, tetanus, stiff neck, spinal convulsion (Ozturk et al., 1996), insomnia (Cott, 1995), hysteria (Zargari, 1990).

3. Previously isolated constituents

Naphthodianthrones (hypericin and pseudohypericin), phloroglucinol compounds (hyperforin and adhyperforin), procyanidins, tannins, coumarins, amino acids and phenylpropanes (Greeson et al., 2001).

4. Materials and methods

In the PTZ test, the aqueous and ethanolic extracts as well as diazepam were injected intraperitoneally 60, 30 and 30 min prior the administration of 90 mg/kg pentylenetetrazole, i.p. (Aldrich, Germany), respectively. The time taken before the onset of clonic convulsions and the percentage of mortality protection were recorded. L-NAME (1, 5 and 10 mg/kg, i.p.) were administered 75 min prior the administration of 90 mg/kg pentylenetetrazole (Vogel and Vogel, 1997). In MES test, an alternating current stimulus of 50 Hz and 150 mA through ear-clip electrodes was delivered for
Table 1

Anticonvulsant effect Hypericum perforatum ethanolic and aqueous extracts in the pentylenetetrazole-induced convulsion in mice

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Onset of seizure</th>
<th>Mortality protection (%) during 30 min</th>
<th>Mortality protection during 24 h (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>10 ml/kg</td>
<td>164.2 ± 38.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diazepam</td>
<td>1 mg/kg</td>
<td>*** 1216.7 ± 17.5</td>
<td>***80</td>
<td>***80</td>
</tr>
<tr>
<td>Ethanolic extract</td>
<td>0.1 g/kg</td>
<td>*** 666.9 ± 110</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>0.4 g/kg</td>
<td>*** 457.1 ± 95</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>0.7 g/kg</td>
<td>*** 227.9 ± 102.7</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>1 g/kg</td>
<td>*** 1052.6 ± 69</td>
<td>60</td>
<td>**60</td>
</tr>
<tr>
<td>Aqueous extract</td>
<td>0.1 g/kg</td>
<td>461.2 ± 94.5</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>0.4 g/kg</td>
<td>*** 293.1 ± 115</td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>0.7 g/kg</td>
<td>*** 662.2 ± 105</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>1 g/kg</td>
<td>*** 925.3 ± 100.3</td>
<td>60</td>
<td>*60</td>
</tr>
</tbody>
</table>

The extracts and diazepam were injected intraperitoneally 30 min prior the administration of pentylenetetrazole (i.p., 90 mg/kg). Values are presented as mean ± S.E.M. for the onset of seizure, n = 10 mice, **P < 0.01, ***P < 0.001, compared to normal saline using Tukey–Kramer test. +P < 0.05, ++P < 0.01, +++P < 0.001, Fisher test.

0.2 s to the experimental animals. A drop of 0.9% saline solution was poured into each ear prior to placing the electrodes. The aqueous and ethanolic extracts as well as diazepam were injected intraperitoneally 60, 30 and 30 min, respectively, prior to the test. The duration of tonic convulsion (a tonic extension of the hindlimb) and the percentage of the mortality protection were recorded (Vogel and Vogel, 1997).

Data were expressed as mean values ± S.E.M. and tested with ANOVA and Tukey–Kramer tests for anticonvulsant activity. The percentage of mortality was assessed by Fisher’s exact test.

5. Results

The maximum non-fatal doses of the aqueous and ethanolic extracts were 1 g/kg. The LD50 values of aqueous and ethanolic extracts were 2.25 g/kg (95% CI: 2.3–4.6) and 3 g/kg (95% CI: 2.2–4.1). Compared with a toxicity classification (Loomis, 1968), the extracts are little toxic. Both the ethanolic and aqueous extracts increased the latency of convulsions induced by PTZ dose-dependently (Table 1). At a dose of 1 g/kg, the extracts produced a protection about 50–60% against mortality (Table 1). Agents affecting the PTZ test can inhibit absence seizures (Vida, 1995). Thus Hypericum perforatum may have some beneficial effect on this kind of seizure in clinical trials. In the MES test, the aqueous and ethanolic extracts did not show anticonvulsant activity. L-NAME (1, 5 and 10 mg/kg) increased the latency of convulsions induced by PTZ, but this effect was not significant. The anticonvulsant activity of the extracts was reduced by L-NAME in PTZ test. L-NAME reduced the antiseizure activity of the extracts. In mice, nitric oxide was produced in response to NMDA receptor activation leads to an increase in cGMP which induces the seizure activity termination (Buisson et al., 1993). It is possible that the anticonvulsant activity of this plant might be partially mediated by nitric oxide pathway. Recently, the effects of different extracts of Hypericum perforatum L. on the kindling epileptic discharges were analyzed (Ivetic et al., 2002). These results support the involvement of nitric oxide pathway in the modulation of seizure by St. John’s wort.

References


