Antinociceptive Profile of 2-Phenylselenenyl-1,8-cineole in Mice

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2-Phenylselenenyl-1,8-cineole (PSC) increased both the pentobarbital-induced sleeping time and the reaction time (up to 2 h) in the tail immersion method. PSC also caused dose-dependent inhibition of acetic acid induced writhing with maximum inhibition of 93.4% and was approximately 8.5-fold more potent than 1,8-cineole. These findings show that PSC presents sedative effect and significant antinociceptive activity.

Key words antinociceptive; terpene; 1,8-cineole; phenylselenenyl

MATERIALS AND METHODS

Chemical Compound PSC was prepared in our laboratory as already described9 and dissolved in 5% Tween 20 as an emulsion.

Animals Male Swiss mice (26—36 g; 6—8 weeks old) were obtained from the Biology Dept. of this University. The animals were maintained at constant room temperature (23±1°C) and on a 12/12 h light–dark cycle (light from 7:00 to 19:00 h), with free access to food and water and for a minimum of 7 d before performing the experiments. All beha
vioral observations were conducted between 13:00 and 19:00 h.

Statistical Statistical analysis was performed by means of variance analysis followed by Student’s t-test or Dunnet’s test. A probability level of 0.01 or 0.05 was accepted as sign|

ificant.

Acute Toxicity and Behavioural Effects The toxicity study was performed with different doses of PSC to groups of mice (n=10) administered intraperitoneal (i.p.), and mortality was recorded for 72 h for the determination of LD50.11) According to the method of Irwin,12) the behaviour of the mice was observed at 1 and 2 h after i.p. injection of PSC.

Pentobarbital-Induced Sleeping Time Sodium pentobarbital at a hypnotic dose of 50 mg/kg was injected i.p. to 2 groups (n=10) of mice 60 min after pre-treatment with 0.9% saline (control) and PSC (30 mg/kg) i.p., respectively. The duration of sleep time (loss and recovery of the righting re|

flex) was recorded.13)

Tail Immersion Method The tail (up to 5 cm) of the mice were dipped into a beaker containing water kept at 50°C. The time for the mice to remove its tail from the hot water was recorded and a maximum 60 s cut-off was used. The mice were divided into 3 groups (n=10). Saline 0.9% (control), PSC (30 mg/kg) and morphine (6 mg/kg) were administered i.p. Readings were taken at 60, 120, 180 and 240 min after drug injection.14)

Acetic Acid Induced Writhing The mice were divided into 6 groups (n=10) and pre-treated with saline 0.9% (control). PSC (15, 30, 60 mg/kg), 1,8-cineole (150 mg/kg) and morphine (6 mg/kg) were administered i.p. After 60 min an acetic acid solution (0.6%; 0.1 ml/10 g) was i.p. injected. After a further 5 min, the number of constrictions was recorded for 5 min.15)

RESULTS AND DISCUSSION

In this work, the effects of PSC were evaluated for central pharmacological activity. PSC did not induce mortality up to a dose of 120 mg/kg in mice. On the basis of animal observation, PSC (30 mg/kg) did not affect the motor coordination, muscle tone and reflexes. However, PSC showed depressant action as observed by decreased locomotor activity, increased passivity and also caused palpebral ptosis at 1 h and 2 h after administration. This central effect of PSC (30 mg/kg) was confirmed by an increase of pentobarbital induced sleeping time (Table 1), indicating a sedative activity. In the evalua|
tion of the analgesic profile, PSC (30 mg/kg) reduced the nociceptive responses in the tail-immersion method (Table 2). The test compound was effective at 60 and 120 min, while the analgesic effect of morphine (6 mg/kg) only lasted up to 60 min. PSC (15, 30, 60 mg/kg) decreased the incidence of acetic acid induced writhing (Table 3). It produced a significant dose-dependent analgesic response. Similarly to morphine (6 mg/kg), PSC (60 mg/kg) showed almost the maximum inhibition for the writhing response. A recently pub-

Table 1. Effect of PSC on Pentobarbital (50 mg/kg, i.p.) Induced Sleeping Time in Mice (Mean±S.E.M.)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose (mg/kg)</th>
<th>Sleeping time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (saline)</td>
<td>—</td>
<td>55.9±4.3</td>
</tr>
<tr>
<td>PSC</td>
<td>30</td>
<td>73.0±6.8*</td>
</tr>
</tbody>
</table>

*p<0.05, n=10.

Notes

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lished report showed that the natural terpene 1,8-cineole presents an analgesic effect, and so we compared the ratio between the doses and the effects of inhibition of PSC (15 mg/kg) and 1,8-cineole (150 mg/kg). PSC was approximately 8.5-fold more active than 1,8-cineole. In conclusion, the present study provides evidence that PSC has a sedative effect and antinociceptive activity, causing both thermal (tail immersion method) and chemical (acetic acid induced writhing) nociceptive stimuli in mice.

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Table 2. Effect of PSC and Morphine on Tail Immersion Test (Mean±S.E.M.)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose (mg/kg)</th>
<th>Reaction time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 h</td>
<td>1 h</td>
</tr>
<tr>
<td>Control (saline)</td>
<td>—</td>
<td>4.0±0.2</td>
</tr>
<tr>
<td>PSC</td>
<td>30</td>
<td>3.9±0.3</td>
</tr>
<tr>
<td>Morphine</td>
<td>6</td>
<td>4.1±0.2</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, n=10.

Table 3. Effect of PSC, 1,8-Cineole and Morphine on Acetic Acid Induced Writhing (Mean±S.E.M.)

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose (mg/kg)</th>
<th>Number of writhings (5 min of observation)</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (saline)</td>
<td>—</td>
<td>24.0±2.5</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>10.7±3.0*</td>
<td>55.4</td>
</tr>
<tr>
<td>PSC</td>
<td>30</td>
<td>4.1±1.1*</td>
<td>82.9</td>
</tr>
<tr>
<td>1,8-Cineole</td>
<td>60</td>
<td>1.6±0.9*</td>
<td>93.4</td>
</tr>
<tr>
<td>Morphine</td>
<td>150</td>
<td>9.3±2.0*</td>
<td>61.2</td>
</tr>
<tr>
<td>Morphine</td>
<td>6</td>
<td>0.0±0.0*</td>
<td>100.0</td>
</tr>
</tbody>
</table>

*p<0.01, n=10.

REFERENCES