Short Communication

Preliminary study on the central nervous system depressant effect of *Picrorhiza kurrooa* Royle. (Scrophulariaceae) in mice models

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SUMMARY

*Picrorhiza kurrooa* Royle. is a well known medicinal plant among the indigenous medical practitioners of India. Present study is the first time to report the activity on the central nervous system. Preliminary study of the hot water extract showed significant depressant activity on the hole board test as evidenced from the ambulation and head dipping scores. The extract showed better activity compared to diazepam on the duration of pentobarbital induced sleeping time. Keywords: *Picrorhiza kurrooa*, CNS, depressant, Hellebore

INTRODUCTION

The prolonged use of modern tranquilizers and psychotrophic drugs lead to a variety of autonomic, endocrine, allergic, hematopoietic and neurological side effects. Moreover, such agents primarily relieve the symptoms and offer a palliative relief of a temporary nature (Koslow et al., 1995). During the last two decades, pharmacotherapy with psychoactive drugs has been increasingly recognized as most effective in the management of anxiety, stress and psychosomatic disorders. In many countries herbal medicines (e.g., St John’s Wort, Valerian) are as commonly prescribed as conventional medications for the treatment of psychiatric problems (Miller and Murray, 1998). The potential of plants as sources for new centrally acting drugs is still largely unexplored, only a small percentage have been investigated phytochemically, and the fraction submitted to biological or pharmacological screening is even smaller (Hamburger and Hostettmann, 1991).

Indian system of medicine has used plants towards the treatment of several ailments in humans for the last 5000 years (Baliga et al., 2003). *Picrorhiza kurrooa* Royle. (English name: Hellebore) is a bitter plant have a remarkable reputation among the indigenous medical practitioners. The plant is well-known in the Ayurveda and has traditionally been used to treat disorders of the
liver and upper respiratory tract (Jadhav and Pal, 2005). There are numerous reports about the hepatoprotective activity of *Picrorhiza kurrooa* and its constituents kutkin and picroliv (Ansari et al., 1988; Ansari et al., 1991; Visen et al., 1991; Visen et al., 1996; Santra et al., 1998). In addition, the plant and its constituents showed anticholestatic (Saraswat et al., 1993), antioxidant (Govindarajan et al., 2003; Vijayakumar et al., 2005), anti-inflammatory (Singh et al., 1993), cyclooxygenase-2 enzyme inhibitory (Zhang et al., 2005), hypolipidemic (Khanna et al., 1994), and immunomodulatory activities (Wang and Pang, 2002; Vijayakumar et al., 2005). Although numerous pharmacological activities have been reported for *Picrorhiza kurrooa*, however no neuropharmacological activity was found on the literature. The present study thus was undertaken to preliminary evaluate the central nervous system depressant activity of *Picrorhiza kurrooa* using mice models.

**MATERIALS AND METHODS**

**Plant materials and extract**
The rhizome of *Picrorhiza kurrooa* Royle. (Family: Scrophulariaceae) was collected from authenticated herbal shop in Dhaka and identified by Mr. M.K. Miah of Bangladesh National Herbarium, Dhaka, Bangladesh where voucher specimens were preserved. The rhizome was then dried and finely powdered by a grinding machine (Mesh size #80). The hot water extract was prepared by boiling 100 g of the powdered plant materials in 1600 ml water and was filtered and evaporated to give 400 ml of hot water extract.

**Animals**
Non-fasted mice (male, Swiss-webstar strain, 20 - 25 g body weight) bred in the animal house of the Department of Pharmacy, Jahangirnagar University, were used for the experiments. The animals were provided with standard laboratory food and tap water *ad libitum* and maintained at natural day night cycle. The animals were grouped (n = 6) according to body weight. The extract was administered orally at a dose of 10 ml/kg. The research was carried out according to the rules governing the use of laboratory animals as acceptable internationally.

**Hole board test**
Experimental method each animal was placed carefully in the center of the field and the number of holes passed, head dipping, and the number of fecal boluses excreted recorded for a period of two min at 0, 30, 60, 120 and 240 min after the oral administration of the extract (Alamgir et al., 2002).

**Pentobarbital-induced sleeping time test**
The extract was administered per oral 30 min before the administration of pentobarbital (i.p.; 40 mg/kg body weight). Diazepam (1 mg/kg i.p.) was used as a positive control. The animals were observed for the onset and the duration of sleep, as evidenced by the observation of the loss of righting reflex (Williamson et al., 1996).

**Statistical analysis**
Unpaired t-tests were performed by SPSS 9.05 to test the level of significance. Probability value of 0.05 or less (p < 0.05) was considered as significant. The data were expressed as a ratio of sleeping time mean value of experimental animals vs. control animals.

**RESULTS AND DISCUSSION**
Intact animals are considered the best method for investigating the action of drugs on central nervous system. Hole board test evokes a pattern of behavior characterized by exploration (head dipping through the holes), locomotion (ambulation past the holes), and emotional defecation. Decrease in sleeping latency and increase in sleeping time are classically related to central nervous system depressant drugs (Williamson et al., 1996). As like
many other centrally active drugs, barbiturates work on the cerebral cortex and thus produce their actions. Pentobarbital, a barbiturate class hypnotic drug by an allosteric modification of GABA<sub>A</sub> receptor increases the chloride conductance and potentiates GABA<sub>A</sub> mediated postsynaptic inhibition (Katzung, 2001). Inhibition of Cytochrome P 450 enzyme system (e.g. CYP1A2, 2C9, 2C19, 2D6, 3A4 and 4A9/11) can lessen pentobarbital metabolism and therefore increase sleeping time (Tsuj et al., 1996).

The hot water extract of <i>Picrorhiza kurrooa</i> significantly (<i>P</i> < 0.01 - <i>P</i> < 0.001) reduced the ambulation of the animals from 30 min to 240 min compared to the control animals (Table 1). The exploratory head dipping behavior was also seen to decreased from 30 min to 240 min (<i>P</i> < 0.01 - <i>P</i> < 0.001). Significant difference was not observed to the defecation compared to control. The findings in this experiment indicate possible central nervous system depressant activity of the <i>Picrorhiza kurrooa</i> extract.

The extract showed a non-significant decrease on the onset of the sleeping time (Table 2) but the duration of the pentobarbital induced sleeping time was significantly increased (<i>P</i> < 0.001). Depressant action (<i>P</i> < 0.001) of the extract is slightly better than the diazepam in terms of the duration of sleep. The findings suggest the action may be attributed to the cerebral mechanism involved in the regulation of the sleep.

At the end of our discussion it must be kept in mind that the compounds present in the extracts are water soluble substances, therefore triterpenoids and flavonoids commonly detected in the extracts might be present in glycosidic forms. On the other hand, it should be considered that other classes of compounds and any other polar substance can be responsible for the central nervous system activity examined in this work (Jiménez et al., 2001). The results given in this paper are a preliminary evaluation of the plant and we suggest other CNS models to further evaluate their potency and bioactivity guided isolation of the pure compound(s).

### Table 1. Effect of <i>Picrorhiza kurrooa</i> on hole board experiment

<table>
<thead>
<tr>
<th>Group</th>
<th>0 min</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
<th>240 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;i&gt;P. kurrooa&lt;/i&gt;</td>
<td>17.16 ± 4.36</td>
<td>4.00 ± 1.54&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.00 ± 4.04&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.66 ± 1.20&lt;sup&gt;a&lt;/sup&gt;</td>
<td>7.00 ± 3.17&lt;sup&gt;a&lt;/sup&gt;</td>
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<table>
<thead>
<tr>
<th>Head Dipping</th>
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</tr>
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<tbody>
<tr>
<td>Control</td>
<td>14.91 ± 0.98</td>
<td>11.58 ± 1.65</td>
<td>13.08 ± 3.04</td>
<td>14.75 ± 2.75</td>
<td>18.25 ± 3.10</td>
</tr>
<tr>
<td>&lt;i&gt;P. kurrooa&lt;/i&gt;</td>
<td>12.00 ± 0.85</td>
<td>1.16 ± 0.74&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.83 ± 1.32&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.50 ± 0.50&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.83 ± 0.54&lt;sup&gt;b&lt;/sup&gt;</td>
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<table>
<thead>
<tr>
<th>Defecation</th>
<th></th>
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<tbody>
<tr>
<td>Control</td>
<td>2.00 ± 0.40</td>
<td>1.08 ± 0.259</td>
<td>0.58 ± 0.19</td>
<td>0.41 ± 0.19</td>
<td>0.33 ± 0.14</td>
</tr>
<tr>
<td>&lt;i&gt;P. kurrooa&lt;/i&gt;</td>
<td>1.83 ± 0.87</td>
<td>0.333 ± 0.33</td>
<td>1.00 ± 0.51</td>
<td>0.66 ± 0.49</td>
<td>1.16 ± 0.54</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± S.E.M. in min<sup>a</sup>
<sup>b</sup><i>P</i> < 0.01, <sup>b</sup><i>P</i> < 0.001

### Table 2. Effect of <i>Picrorhiza kurrooa</i> on the hypnotic action of pentobarbital

<table>
<thead>
<tr>
<th>Group</th>
<th>Onset of sleep</th>
<th>Duration of sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>353.8 ± 68.7</td>
<td>2519.1 ± 261.2</td>
</tr>
<tr>
<td>&lt;i&gt;P. kurrooa&lt;/i&gt;</td>
<td>230.0 ± 24.0</td>
<td>6380.0 ± 607.0&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diazepam (1 mg/kg)</td>
<td>243.6 ± 16.2</td>
<td>5000.4 ± 139.8&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± S.E.M. (<i>n</i> = 6) in sec<sup>a</sup><i>P</i> < 0.001

### REFERENCES


Ansari RA, Aswal BS, Chander R, Dhawan BN, Garg...
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