The present study was designed to evaluate the toxic and non toxic profile of Ipomoea hederacea (Convolvulaceae). The results of oral toxicity study was observed in mice at the doses of 300, 200, 100, 50, 25, 10, 1, 0.025 and 0.0125 mg/kg. The starting of lethal effect was recorded at the dose of 300 mg/kg and the calculated LD₅₀ value was found 229.2 mg/kg dose. The toxic sign and symptoms after oral dose introduction in mice were convulsion and tremor. Dose dependent toxic effect in behaviour of mice included convulsion, tremor, unsteady gait, and respiratory distress to death. It was also observed that at the dose of 1, 0.025, 0.0125 no sign of toxicity in behaviour of animal was observed and the calculated ED₅₀ was found 0.0125-lmg/kg. In analgesic activity test at low dose (1, 0.025, 0.0125 mg/kg) significant reduction in number of writhes were observed (p< 0.05). Hot plate analgesic activity was also exhibited some analgesic potential.

**Key words:** LD₅₀, ED₅₀, Ipomoea Hederacea, Toxicity

**INTRODUCTION**

Ipomoea hederacea belongs to the family convolvulaceae used as a phytomedicine [1]. The aim of the present study was to evaluate the toxic and non toxicological behaviour with respect to dose. We also report the LD₅₀ and ED₅₀ in mice, in order to increase the confidence for safe use to humans. Since literature survey indicates the negligence of this herb (Ipomoea hederacea) for its medicinal and pharmacological action, there fore different pharmacognostic and pharmacological experiments were carried out to explore its medicinal value beside its poisonous category.

**MATERIAL AND METHOD**

**Plant material**
The seeds of Ipomoea hederacea (2.5kg) were purchased from local market and the voucher specimen no. RIPPS-0210-0208, was deposited in the herbarium of Research Institute of Pharmaceutical Sciences, Department of Pharmacognosy, University of Karachi, Pakistan. The seeds were ground coarsely and soaked in methanol for two weeks. The methanol extract was filtered and evaporated under reduced pressure in a rotary evaporator to yield crude extract (10gm).

**Test animals**
Two groups (control and treated) of albino mice of positive NMRI strain of either sex and of same weight (i.e. 25-30 g) were selected for different experiments (each group comprises of 5 animals). The animals were purchased from HED Research Institute of Chemistry, University of Karachi, Karachi. Pakistan. Animals used for CNS activity were acclimatized first for at least 5 days in the laboratory environment with 12 hours light and 12 hours dark schedule. Animals were housed in standard metal cages and provided food and water ad-libitum.

**Preparation of test material**
The dose of methanol crude extract of Ipomoea hederacea was prepared in 0.5 ml distilled water i.e. 0.0125, 0.025, 1, 25, 50, 75, 100, 200, 300 mg/kg/0.5ml and 500 mg/kg/0.5 ml.

**Phytochemical analysis**
The presence of saponins, tannins, terpenes, alkaloids, proteins etc were detected by simple qualitative methods [2, 3].

**Gross behavioural study**
For monitoring the effects of crude extract of Ipomoea hederacea on central nervous system, the procedure was adopted as described by Irwan 1964 and Debprasad et al., 2003 [4, 5].

**Assessment of neuropharmacological activity**
CNS activity was studied by open field test [6, 7], cage cross [8], head dip, rearing test, traction test and swimming induced depression test [9, 10, 5]. All the CNS related tests were performed according to the procedure described in literatures.

In each test, animals were divided into different groups (Group-A for control, Group-B1-11 for oral doses (0.0125,0.25, 1, 5, 10, 25, 50, 75, 100, 200, 300 mg/kg) of crude extract respectively, and Group-C for standard). Each group comprised of 5 animals. Aspirin 300 mg/ kg, Diazepam 2mg/kg and Imipramine 10 mg/kg orally were used as standard. The crude drug and the diazepam were diluted in distilled water and administered orally. The control animals were treated orally with the same volume of saline as the crude extract. In all tests observations were made after 30 to 40 minutes of oral dose of the test substance.

**Statistical analysis**
Values for observations were expressed as mean after drug administration ± SEM. The significance of difference between means was determined by Dunnett’s t-test and values of P < 0.05 were considered significant. All statistical procedure was performed according to the method of Alcaraz and Jimenez, 1989[17].

**RESULTS**

**Phytochemical analysis**
The presence of different chemical constituents in methanolic crude extract of seeds of Ipomoea hederacea is identified by reactions with various chemical reagents. Thin layer chromatography of Ipomoea hederacea aqueous extract is performed in two different solvent systems (Table 1).

<table>
<thead>
<tr>
<th>Solvent system</th>
<th>Rf value</th>
<th>Chemicals</th>
<th>Positive drug reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloroform-Methanol-Water (80:20:2)</td>
<td>0.30;0.59;0.64;0.73</td>
<td>Carbohydrates(++)</td>
<td>Water Brown</td>
</tr>
<tr>
<td>Ethylacetate-Methanol-Water (100:15:5)</td>
<td>0.32;0.51;0.62</td>
<td>Proteins (+++)</td>
<td>HNO₃ Yellowish green</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alkaloids(++)</td>
<td>FeCl₃ Greenish blue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Triterpenoids(++)</td>
<td>Conc. KOH Reddish brown</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sterols(++)</td>
<td>Dull yellow</td>
</tr>
</tbody>
</table>

**acids**

**Table 1:** Phytochemical studies of Crude extract of Ipomoea hederacea

**Table 2a:** Acetic acid induced writhing test

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Mean No. of writhes</th>
<th>% of inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.5ml saline</td>
<td>123±2.48</td>
<td>-</td>
</tr>
<tr>
<td>Cl</td>
<td>1</td>
<td>53±2.36</td>
<td>56.9*</td>
</tr>
<tr>
<td></td>
<td>0.025</td>
<td>59±2.16</td>
<td>52.0</td>
</tr>
<tr>
<td></td>
<td>0.0125</td>
<td>72±1.96</td>
<td>43.1Aspirin 300</td>
</tr>
<tr>
<td></td>
<td></td>
<td>46±1.27</td>
<td>62.2*</td>
</tr>
</tbody>
</table>

* Each value is the mean ± S.E.M. of five determinations. *P < 0.05, Dunnet test as compared to control

**Table 2b:** Acetic acid induced writhing test

**Table 2a:** Acetic acid induced writhing test

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**ABSTRACT**

The present study was designed to evaluate the toxic and non toxic profile of Ipomoea hederacea (Convolvulaceae). The results of oral toxicity study was observed in mice at the doses of 300, 200, 100, 50, 25, 10, 1, 0.025 and 0.0125 mg/kg. The starting of lethal effect was recorded at the dose of 300 mg/kg and the calculated LD₅₀ value was found 229.2 mg/kg dose. The toxic sign and symptoms after oral dose introduction in mice were convulsion and tremor. Dose dependent toxic effect in behaviour of mice included convulsion, tremor, unsteady gait, and respiratory distress to death. It was also observed that at the dose of 1, 0.025, 0.0125 no sign of toxicity in behaviour of animal was observed and the calculated ED₅₀ was found 0.0125-lmg/kg. In analgesic activity test at low dose (1, 0.025, 0.0125 mg/kg) significant reduction in number of writhes were observed (p< 0.05). Hot plate analgesic activity was also exhibited some analgesic potential. Other studies like open field, exploratory behaviour, forced swimming test for stress and insecticidal activity were also carried out on the crude methanolic extract of this plant.
**Table 4: Toxicity (in terms of convulsions) and percentage mortality of crude extract of D. hederacea**

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>No. of survivor</th>
<th>Immobility time (sec)</th>
<th>% Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>300</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>200</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>50</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
<tr>
<td>Aspirin</td>
<td>4</td>
<td>&gt;0.22</td>
<td>0</td>
</tr>
</tbody>
</table>

Each value is the mean ± S.E.M. of five determinations.

**DISCUSSION**

The literature survey reveals that *Ipomoea hederacea* is an important medicinal plant because of its uses in the cure of different diseases. But a prominent character is the effect on thread worms where it kills or repels intestinal worms [18]. During this study the chemical reactions and other related tests were performed to standardized the crude extract. The drug showed the presence of alkaloids, triterpene, tannins and protein.

The analgesic activity of plant extract was performed in mice and the drug was found significantly reduce the pain response at 1-0.025 mg/kg when compared with aspirin 300 mg/kg (hot plate test: 0.23±0.09, and 0.40±0.025; and acetic acid induced writhing test: % of inhibition 56.9 and 52 respectively at p<0.05). This is because of co-relation with the CNS depressant effects of the extract. Pain can be relieved centrally as well as peripherally [19]. Generally there are two major types of peripheral acting analgesics, that are absent the activation (sensitization) of nociceptors and those, which directly down regulate activated (sensitized) nociceptors [20]. NSAIDs like aspirin subsides pain by inhibiting synthesis of prostaglandins. Prostaglandins produce inflammation by a number of mechanisms and also make the nociceptors more sensitive to pain producing agents such as bradykinin [19]. This shows that aspirin also prevents the activation of peripheral nociceptors.

Gross behaviour studies was performed to evaluate changes occurs upon the administration of drug in mice behaviour. The extract showed slight irritability and alertness at the dose of 1mg/kg and 0.025mg/kg and 0.0125mg/kg. The drug showed the toxic profile at other doses. The CNS stimulating activity could be helpful to decrease anxiety and panic state in the patient. In present study *Ipomoea hederacea* increases open field, improves head dip and rearing activities, which indicate these effects on locomotion and exploration. All psychotropic drugs increases locomotion and exploratory behavior may be used in the treatment of neurological disorders.

Traction test is the useful technique for the determination of effect of drug on muscles activity. Upon the administration of crude extract of *Ipomoea hederacea* mice showed the increase in the time of distance travelled at the doses of 0.025 mg/kg and 0.0125 mg/kg but at other doses all mice failed in traveling and fall from the rod. This indicated the effect of drug on the muscles activity at low dose. This result was supported by other activities performed on the extract. During forced swimming test at low dose less significant effect on mobility time was observed (antidepressant) but at high dose mice can not swim rather static response observed.

The results of the oral acute toxicity indicated that there was 50% mortality at higher dose. However, the treated mice showed signs of convulsions, paralysis and tremors. Death occurring in groups that received 300, 200 and 100 mg/kg within 14 h of extract administration while all the animals treated with 300 mg/kg group died within 24 h. The mortality rates and calculated LD₅₀ are presented in Table 4. Gross toxicological and non toxicological behaviour were observed at different doses, crude extract of rats are shown in tables. Oral LD₅₀ of drug is 229.2mg/kg and ED₅₀ is 0.0125mg/kg. Therefore the dose dependent toxic manifestations present in the extract, where the mortality increases with the increase in concentration.

Strychnine produces tetanus-like convulsions. Feeling of suffocation, during paroxysms eyes-balls prominent, pupils dilated, respiration impeded, pulse feeble and very rapid. Intelect generally clear. Hearing and sight keen. The convulsions do not involve the jaw muscles until late, whereas in tetanus these muscles are affected early [21]. The crude extract produces the similar action in mice thus can be included a one of the excitatory neurotransmitter probably glycine.

Insecticidal activity was performed to evaluate the toxic principles present in the plant. Significant activity was seen by the crude extract at 300, 200, 100, 50, 25, 1, 0.025 and 0.0125 mg/kg dose against the tested pest i.e. *Tribolium castaneum* (Table 5).

The crude extract and its different doses showed insecticidal activities against *Tribolium castaneum*. At the dose of 300-0.01 mortality is 100%, 0.001mg showed 0% mortality; however, these results are time dependant.

Many of insectsicides in today use are organophosphorous (OP) or carbamate cholinesterase inhibitors. OP nerve agents were used in both chemical warfare and terrorist attacks during the preceding decade. Paradoxically, the carbamate cholinesterase inhibitor pyridostigmine has been used to increase the efficacy of antidotes to OP nerve agents by temporarily “protecting” the active site of Acetyl choline esterase (AChE) [21]. Since the drug has powerful insecticidal effect so it can be used in the replacement of these agents. The assessment of toxicity is not limited the use rather it may be applied to all the possible therapeutic effect at lower dosage. Such kind of results helpful in the treatment of diseases.

**CONCLUSION**

The findings of the present study are encouraging, since the crude extract of *Ipomoea hederacea* at lower doses showed a promising analgesic, CNS stimulant activity and potential towards improvement of muscles activity. Analgesic and neuropharmacological activities were significant both at 1mg/kg and 0.025 mg/kg and 0.0125 mg/kg doses, which were comparable with the reference drug aspirin and diazepam. The finding is corroborated by our result that the test substance inhibited the acetic acid induced writhing in mice and increases the pains threshold by hot plate method. The most pronounced effect was produced at 1 mg/kg after one hour.
which then started to decrease after 2 hours with out the hazards of toxicity. The results of analgesic activity (Writhing test) were significant as the mean number of writhes for control was 123 and that for 1 mg/kg and 0.025 mg/kg and 0.0125 mg/kg doses of crude extract was 56.9 and 52 and 43.1 respectively. These finding reflect that drug has analgesic effect more at 1 mg/kg while less on 0.0125 mg/kg.

These interesting results are presented in this report indicate that Ipomea hederacea may have useful effects in various neurodegenerative diseases. Further studies are in progress to confirm the mechanism of action with other experimental models.

REFERENCE

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