EFFECTS OF LANTANA ACULEATA ROOT EXTRACT ON LIVER ENZYMES IN RATS

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ABSTRACT
Lantana aculeata (Verbenaceae) is a weed distributed throughout the Indian subcontinent. The leaves of the plant are reported to be hepatotoxic, while the roots were hepatoprotective. Hence an attempt has been made to study the effects of the roots with its ethanolic extract on liver enzymes in rat model. The extract was orally given to seven groups at the doses of 50, 100, 200, 400, 800, 1600 and 3200 mg/kg for short and long term of 30 and 60 days. The results revealed no changes in the liver enzymes of Aspartate aminotransferase (AST), Alanine transferase (AST) and Alkaline phosphatase (ALP) in animals treated with 50 mg/kg for 30 days. For 60 days, the liver markers exhibit elevated levels in all doses treated when compared to control animals. This suggests that Lantana aculeata root extract does not show any toxicity in lower dose for short term administration and its safety is concluded in lower dose for shorter duration.

KEYWORDS Lantana aculeata roots, liver enzymes, rats

INTRODUCTION
Lantana aculeata (Verbenaceae family), a widely growing shrubby weed blossoms throughout the year in India [1] The leaves of the plant found to cause hepatotoxic disease in grazing animals, [2] while roots have application as oral drug for human liver disorders. [3] However, no report on its toxicity has been made. Therefore to obtain safety data of roots prior to clinical trial, short and long term toxicity study was performed in rats.

MATERIALS AND METHODS
Plant Material
Mature roots of Lantana aculeata (Verbenaceae) were collected during the month of October – November from Puducherry (India). The plant material was identified and authenticated by Dr. P. Jayaraman, Director, Plant Anatomy Research Centre, Medicinal Plant Research Unit, Chennai (India). A voucher specimen has been deposited for future reference (No. PARC/2006/8).

Extraction
Plant material (about 1 kg) was cut into small pieces, shade dried, coarsely powdered and exhaustively extracted with ethanol by cold percolation method. After 72 hours, the solvent was decanted and distilled-off over the boiling water-bath. Further concentrations were done under reduced pressure using rotary flash evaporator and finally dried in a dessicator. The yield of the extract was noted to be 0.32% (w/w).

Animals and treatment
Adult male albino rats of Wistar strain weighing 150 - 200 g used for the study were obtained from Tamil Nadu University of Veterinary and Animal Sciences, Chennai (India) and maintained according to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals, Chennai (India) (Reg. No. 324). The permission of the Departmental Ethical Committee was obtained for the study and the experiment was conducted as per the principles prescribed for laboratory animal
use. Animals were fed with commercial pelleted chow obtained from Poultry Research Station, Chennai (India) and water was provided *ad libitum.*

**Toxicity Studies**

The doses for the study were selected on the basis of lethal dose 50% of *Lantana aculeata* root extract, which found higher than 3200 mg/kg of body weight. Hence, a descending sequence of dose level was selected with an aim to demonstrate a dose related response. Thereafter, the animals were acclimatization for a week and divided into two sets for short and long term toxicity studies.

**Short-term**

Animals were segregated into 8 groups (n=6), consisting of one control and seven *Lantana aculeata* root extract treated with doses of 50, 100, 200, 400, 800, 1600 and 3200 mg/kg continued for 30 days. The rats were observed closely for any death and morphological changes.

**Long-term**

A second set of animals were divided into 7 groups (n=6) with one control and six *Lantana aculeata* root extract treated with doses of 50, 100, 200, 400, 800 and 1600 mg/kg for 60 days continuously. The animals were noted for any mortality and chronic effect.

**Biochemical analysis**

The two sets of animals were sacrificed on day 31 and 61 respectively by cervical decapitation. The blood was collected and serum has been separated. Standard methods were employed to determine the liver markers such as Aspartate aminotransferase (AST),[^4] Alanine transferase (AST),[^5] and Alkaline phosphatase (ALP)[^6] coupled with Randox Daytona fully automated random axis analyzer (United Kingdom) in the serum of the experimental animals.

**STATISTICAL ANALYSIS**

Data obtained were subjected to ‘t’ – test and expressed as mean ± standard deviation. Values with *p* < 0.01, *p* < 0.001, *p* < 0.05 were considered significant.

**RESULTS**

The LD₅₀ were found to be greater than 3200 mg/kg/day in this study. *Lantana aculeata* root extract did not produce any significant changes in the autonomical and behavioral responses for both the duration. In 30 days treatment, 50% of the animals suffered lethal effect on day 21 with 3200 mg/kg dose treated. No mortality was noted in all doses studied for long-term. In short term study, the liver enzymes AST and ALT remain unaltered in lower dose (50 mg/kg of body weight) and showed increase in intermediate and higher doses. Both AST and ALT levels started increase in a dose-dependant manner during 60 days when compared to normal rats. The levels of ALP is found to be decreased in lower doses for both the periods, the same started increase in dose-dependent manner for remaining doses when compared to control animals (as shown in table-1).

The result indicated that ethanolic extract of *Lantana aculeata* roots given orally at the dose of 50 mg/kg did not produce any sign of toxicity in the rats during short term administration.

**DISCUSSION**

Weeds are generally considered to be irrelevant and destroyed due to their notorious properties. Considering the wide availability of weeds this work focused on *Lantana aculeata*. The root of the plant occupies its position in various traditional practices and reported to possess higher concentration of oleanolic acid which exhibit potent hepatoprotective activity.[^7] As no detailed information on roots toxicity is available, the present study focused on the biochemical effects on liver enzymes in rats.
Table No 1: Effects of Lantana aculeata root extract on the liver enzymes of rats treated for 30 and 60 days.

<table>
<thead>
<tr>
<th>Treatment (mg/ kg)</th>
<th>AST (mg/ dl)</th>
<th>ALT (mg/ dl)</th>
<th>ALP (mg/ dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 Days</td>
<td>60 Days</td>
<td>30 Days</td>
</tr>
<tr>
<td>Group – I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>122.66 ± 3.32</td>
<td>122.66 ± 3.32</td>
<td>33.50 ± 3.61</td>
</tr>
<tr>
<td>Group – II</td>
<td>115.00 ± 3.67</td>
<td>153.67 ± 2.73</td>
<td>31.67 ± 2.34</td>
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<tr>
<td>(50 mg/ kg)</td>
<td></td>
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<tr>
<td>Group – III</td>
<td>122.67 ± 4.50</td>
<td>NS</td>
<td>174.67 ± 3.72</td>
</tr>
<tr>
<td>(100 mg/ kg)</td>
<td></td>
<td></td>
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<tr>
<td>Group – IV</td>
<td>143.00 ± 3.74</td>
<td>177.17 ± 5.17</td>
<td>55.17 ± 3.71</td>
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<tr>
<td>(200 mg/ kg)</td>
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<tr>
<td>Group – V</td>
<td>179.17 ± 3.48</td>
<td>205.67 ± 3.26</td>
<td>60.83 ± 3.43</td>
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<tr>
<td>(400 mg/ kg)</td>
<td></td>
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<tr>
<td>Group – VI</td>
<td>205.00 ± 3.69</td>
<td>259.17 ± 3.26</td>
<td>76.83 ± 3.43</td>
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<tr>
<td>(800 mg/ kg)</td>
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<tr>
<td>Group – VII</td>
<td>225.50 ± 3.39</td>
<td>271.83 ± 3.26</td>
<td>89.00 ± 3.54</td>
</tr>
<tr>
<td>(1600 mg/ kg)</td>
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</table>

Values represent mean ± SD of six animals.
*P < 0.05, **P < 0.01, ***P < 0.001; NS - Non-significant when compared to control animals.

Aspartate aminotransferase (AST), Alanine transferase (ALT) and Alkaline phosphatase (ALP)

In short term study, with 3200 mg/kg, 50% of the animals suffered lethal effect on day 21, revealed the toxic nature of the dose administered. The liver enzymes AST and ALT suggest liver impairment and reliable indices of liver toxicity [8]. Both AST and ALT increased in higher doses could be an indication of hepatocellular changes.

In long term study both AST and ALT found elevated when compared to control group rats clearly revealed the toxic nature of the root extract for prolonged administration.

Raise in level of ALP is usually a characteristic finding for liver diseases [9]. The significant reduction of ALP levels in short and long term study at lower doses showed no possible occurrence of any major hepatocellular damage. The elevation in the enzymes is likely a result of the liver inability to metabolize large amount of phytochemical compounds present in higher doses of the Lantana aculeata root extract.

CONCLUSION

It is concluded that the Lantana aculeata root extract at lower dose for shorter duration does not produce any significant toxic effect. This kind of study will help in the fruitful utilization of weeds for the benefit of the society and give a new direction in drug research.
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REFERENCES