EVALUATION OF ANTI-ULCER ACTIVITY OF AERVA LANATA STEM EXTRACT IN RATS

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ARTICLE INFO
Article history
Received 15/11/2013
Available online
31/12/2013

Keywords
Aerva lanata,
Anti-Ulcer Activity,
Pyloric Ligation,
Ethanol Induced Ulcers,
Cysteamine induced Ulcers,
Indomethacin Induced Ulcers,

The anti-ulcer effect of aqueous extract of Aerva lanata stem was tested against ulcers induced by ethanol, pyloric ligation, indomethacin and cysteamine in wistar albino rats. The anti-ulcer activity was assessed by determining and comparing the ulcer index in the test group (250,500 mg/kg) with that of the control group and omeprazole 20mg/kg was used as a reference standard. Aerva lanata significantly decreased free-acidity, total-acidity, ulcer index and increased the pH in pylorus ligated model where as ulcer index decreased in ethanol, indomethacin and cysteamine induced models. One of the more significant findings to emerge from this study is that aqueous extract of Aerva lanata stem possess antulcer properties in a dose dependent manner which could be either due to cytoprotective action, anti secretory or anti oxidant mechanism of the drug. The antulcer properties of the extract may be attributed to the presence of phyto chemicals like flavonoids, alkaloids and tannins present in the plant extract with various biological activities.

Please cite this article in press as Rajitha Indukuri et al. Evaluation of anti-ulcer activity of aerva lanata stem extract in rats. Indo American Journal Of Pharm Research.2013;3(12).

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INTRODUCTION

Peptic ulcer is an excoriated area of the gastric or duodenal mucosa caused by action of the gastric juice. It is a chronic and recurrent disease, and is a very common global health problem today [1, 2]. The exact causes of peptic ulcer disease are not known but it may be result from an imbalance between acid-pepsin secretion and mucosal defence factors [3]. There are 350,000 to 500,000 new cases per year and more than one million ulcer related hospitalization each year [4]. Number of drugs including proton pump inhibitors, prostaglandin analogs, histamine receptor antagonists and cytoprotective agents are available for the treatment of peptic ulcer. But most of these drugs produce several adverse reactions including toxicities and even may alter biochemical mechanisms of the body upon chronic usage [5].

A new approach would be the use of cytoprotective agents that can also modulate the antioxidant defenses in the body and thus prevent mucosal damage and gastric ulceration. As plants are a rich source of active principles and antioxidants, there has been a growing interest to identify and scientifically validate agents that have traditionally been used in folk medicine in the treatment of gastric ulcers and related diseases [6].

*Aerva lanata* is a medicinal plant belonging to the *Amaranthaceae* family. It is widely spread in the drier parts of the tropics and the sub tropics of the world. *Aerva lanata* is commonly described in ayurveda as a diuretic with anti-inflammatory, anti helminthic, anti-bacterial and mild analgesic effects. It is used in the treatment of lithiasis, cough, asthma, and headache and as an antidote for rat poisoning [7, 8]. In the district of Rajasthan *Aerva lanata* roots used to treat jaundice, biliousness and snake bite treatment. The whole plant is used to treat dyspepsia, pneumonia, typhoid and other prolonged fevers [9, 10]. In addition to the traditional uses, the plant is reported for a number of pharmacological activities viz., demulcent, anti-diabetic, anti-hyperglycemic, anti-microbial, cytotoxic, urolithiatic, and hypoglycemic, anti hyper lipidemic, anti-parasitic and anti -helminthic activities [11]. However there are no reports on the antiulcer activity of the *aervalanata* stem. Hence the present study was designed to investigate its anti ulcer activity.

MATERIAL AND METHODS

Plant Material

The stems of the plant were collected in the month of June, 2011 from Narsapur forest, Medak. The plant was identified and authenticated. A herbarium specimen of the plant was preserved in the department of Pharmacognosy of our institute for further reference.

Preparation of Extracts

The stems of the plant were shade dried, powdered mechanically and subjected to soxhlet extraction successively with distilled water. After extraction the filtrate was concentrated on a rotary evaporator under vacuum at 20°C till a residual mass was obtained. Ten grams of the dried extract was triturated with 9 ml of vehicle. Vehicle was then added gradually until the final concentration of the extract was 10%.

From the literature review, it was found that the active constituents (phenolic compounds, saponins, flavonoids, tannins and phyto sterols) present in the *Aerva lanata* are soluble in aqueous solvent [12]. Hence, the present study used aqueous extract.

Experimental Animals:

Healthy male Wister albino rats at 8 weeks of age were purchased from Ghosh Enterprises, Kolkata. They were housed in a room, maintained at approximately 25 ± 2°C, the photo period was 12 hrs light and 12hrs dark cycle. For feeding, the rodent laboratory diet used which is supplied from Ryan biotechnology pvt ltd. Hyderabad. The study was performed following approval from Institutional Animal Ethical Committee (IAEC) of Vishnu Institute of Pharmaceutical Education and Research, Narsapur, Medak. (1358/ac/10/CPCSEA). Ethical norms were strictly followed during all experimental procedures.

Acute Toxicity Studies:

Acute toxicity studies for aqueous extract of *Aerva lanata* stem was determined as per the OECD guideline no.423 (acute toxic class method). It was observed that the stem extract was not lethal to the rats even at 2000mg/kg dose. Hence we selected 250mg/kg and 500mg/kg of this dose for further study [13].

ANTI ULCER ACTIVITY:

Ethanol Induced Ulcer

The experiment was performed according to the method of morimoto et al., with minor modifications [14]. All the animals were fasted for 12 hours before administration of ethanol. The animals were divided into four groups of six animals each. First group was given 1ml of vehicle (distilled water). The second group was treated with 250 mg/kg, of *Aerva lanata* and the third group was treated with 500mg/kg of *Aerva lanata*. The remaining group received omeprazole, in the dose of 20 mg/kg. The gastric ulcers were induced in all groups by administrating absolute ethanol (90%) (1ml/200g) orally, after 60 min of *Aerva lanata* extract and omeprazole treatment. One hour later, the animals were sacrificed by cervical dislocation, and stomachs were incised along the greater curvature and ulceration will be scored.

Pyloric Ligation in Rats

Animals were divided into four groups, each consisting of six rats. Rats in group I, served as control group, received distilled water (1 ml) orally. Group II & group III treated with 250 mg/kg, 500mg/kg of aqueous extract of *Aerva lanata* respectively. Rats in group IV received omeprazole at dose of 20 mg/kg. Pyloric ligation was done according to the method of Shay H et al., [15]. It was done by ligating the pyloric end of the stomach of rats 1 hour after drug adminstration. Ligation was done without causing any damage.
to the blood supply of the stomach. The animals were sacrificed after 4 hours of surgery, by cervical dislocation and the ulcer index were examined.

**Indomethacin Induced Gastric Ulcers**

Non-steroidal anti-inflammatory agents, like indomethacin induce gastric lesions by inhibition of cyclo-oxygenase produced in the gastric mucosa. Animals were divided into four groups, each consisting of six rats. First group was treated with 1ml of vehicle (distilled water). Group ii & iii treated with 250 mg/kg, 500mg/kg of Aerva lanata extract and group iv treated with omeprazole (20 mg/kg). After 60 min gastric ulcers were induced with oral indomethacin at a dose of 40 mg/kg [16]. Four hours later, the rats were sacrificed. The stomachs were removed and examined for ulcer spots.

**Cysteamine Induced Duodenal Ulcers**

Duodenal ulcer was induced by administering cysteamine hydrochloride (400mg/kg p.o) twice, at interval of four hours [17]. Test drug was administered 30 min prior to each dose of cysteamine hydrochloride. After 24 hr all the animals were sacrificed and the duodena were excised carefully and cut open along the anti mesentric side. The duodenal ulcer spots and ulcer index were determined.

**Measurement of Ulcer Index**

Stomach was incised along the greater curvature and the mucosa was rinsed with normal saline to remove blood contaminant. The sum of the length (mm) of all lesions for each stomach was used as the ulcer index. The percentage of inhibition was calculated by the method described by nguele fack et al. [18]

\[
\% \text{Inhibition} = \left( \frac{\text{USC} - \text{UST}}{\text{USC}} \right) \times 100
\]

USC = ulcer surface area in control.
UST = ulcer surface area in treated.

**Determination of Free and Total Acidity in Pyloric Ligation Induced Rats**

Gastric juice was collected from the pylorus-ligated rats. The gastric juice thus collected was centrifuged and the volume of gastric juice as well pH of gastric juice was measured. 1ml of gastric juice was pipetted into a 100 ml conical flask; added 10ml of distilled water and the pH of this solution were noted. Then added 2 to 3 drops of to pfer’s reagent and triturated with 0.01n NaOH (previously standardized with 0.01n of oxalic acid) until all traces of the red colour disappears and the colour of solution was yellowish orange. The volume of alkali added was noted. The volume corresponds to free acidity. Then 2 to 3 drops of phenolphthalein solution was added and titration was continued until a definite red tinge reappears. Again the total volume of added was noted. The volume corresponds to total acidity.

**Acidity Was Calculated By Using The Formula:-**

\[
\text{Acidity} = \frac{\text{Volume of } \text{NaOH} \times \text{Normality of } \text{NaOH} \times 100}{0.1} \text{ meq/l/100g}
\]

**Statistical Analysis**

The values are represented as mean ± SEM, and statistical significance between treated and control groups was analyzed using of one way Anova,[19] followed by Dunnett’s test [20] where as values less than 0.05 were considered as statistically significant.

**RESULTS**

**Acute Toxicity Studies:**

The extract was found to be safe in the dose used and there was no mortality up to a dose of 2000 mg/kg body weight. It was found that even at 2000mg/kg dose did not manifest any significant abnormal signs, mortality, behavioral changes, and body weight changes. Toxicity signs such as tremors, salivation, diarrhea and lethargy were not observed. Confirming practically these are not has toxic activity.

**Effect of Aqueous extract of Aerva lanta on Ethanol Induced Gastric Ulcers**

A significant increase of percentage inhibition was observed in extract-treated groups (49.32%, 62.03% for 250mg/kg and 500mg/kg respectively) compared to the vehicle-treated group. Percentage inhibition was significantly increased in the 500mg/kg of Aerva lanta aqueous extract treated group; it’s also showed significant anti ulcer activity, which was comparable with standard drug omeprazole (table 1).

**Tabel-1: Effect of Aqueous Extract of Aerva lanta In Ethanol Induced Gastric Ulcers**

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<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Ulcer Index</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>16.12±0.12</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>Aerva lanta (250mg/kg)</td>
<td>8.13±0.31</td>
<td>49.32</td>
</tr>
<tr>
<td>III</td>
<td>Aerva lanta (500mg/kg)</td>
<td>6.12±0.24</td>
<td>62.03</td>
</tr>
<tr>
<td>IV</td>
<td>omeprazoles (20mg/kg)</td>
<td>4.28±0.17</td>
<td>73.44</td>
</tr>
</tbody>
</table>

Effect of Aqueous Extract of *Aerva lanta* in Ethanol Induced Gastric Ulcers

The aqueous extract of *Aerva lanta* pretreated group depicted marked reduction in gastric lesion as compared to control. Extract treated group was showing protection index of 38.67% and 70.81% at the dose of 250 and 500 mg/kg respectively in comparison to control whereas omeprazole as reference standard drug was reduction of ulcer 76.56% (table 2).

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Ulcer Index</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>20.18±0.32</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>Aerva lanta (250mg/kg)</td>
<td>8.34±0.19</td>
<td>58.67</td>
</tr>
<tr>
<td>III</td>
<td>Aerva lanta (500mg/kg)</td>
<td>5.89±0.23</td>
<td>70.81</td>
</tr>
<tr>
<td>IV</td>
<td>omeprazoles (20mg/kg)</td>
<td>4.73±0.11</td>
<td>76.56</td>
</tr>
</tbody>
</table>

Effect of Aqueous Extract of *Aerva lanta* in Indomethacin Induced Gastric Ulcers

Graph-1: Effect of Aqueous Extract of *Aerva lanta* in Ethanol Induced Gastric Ulcers

Graph-2: Effect of Aqueous Extract of *Aerva lanta* in Indomethacin Induced Gastric Ulcers
Effect of Aqueous Extract of *Aerva lanta* in Pyloric Ligation Induced Gastric Ulcers

The rat pretreated with *Aerva lanta* aqueous extract (500mg/kg) produced significant decrease in ulcer index, gastric volume. As well as *Aerva lanta* extract also significantly reduces free acidity, total acidity. Whereas, pH was significantly increased when compared with control group. Omeprazole also show similar effects but was more effective compared with *Aerva lanta* (table 3).

### Table 3: Effect of Aqueous Extract of *Aerva lanta* in pyloric Ligation Induced Ulcers

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Gastric Secretion (Meq/L/100g)</th>
<th>pH</th>
<th>Free Acidity (Meq/L/100g)</th>
<th>Total Acidity (Meq/L/100g)</th>
<th>Ulcer Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>2.981±0.031</td>
<td>2.371</td>
<td>231.31±5.342</td>
<td>522.13±9.120</td>
<td>19.39±0.22</td>
</tr>
<tr>
<td>II</td>
<td><em>Aerva</em> (250mg/kg)</td>
<td>2.126±0.068</td>
<td>2.681</td>
<td>168.72±8.921</td>
<td>483.70±18.126</td>
<td>9.20±0.11</td>
</tr>
<tr>
<td>III</td>
<td><em>Aerva</em> (500mg/kg)</td>
<td>1.013±0.017</td>
<td>2.980</td>
<td>138.01±11.345</td>
<td>428±3.341</td>
<td>6.12±0.41</td>
</tr>
<tr>
<td>IV</td>
<td>Omeprazole (20mg/kg)</td>
<td>1.214±0.126</td>
<td>3.452</td>
<td>126.12±10.761</td>
<td>460.12±12.361</td>
<td>4.89±0.35</td>
</tr>
</tbody>
</table>

Effect of Aqueous Extract of *Aerva lanta* in Cysteamine Induced Peptic Ulcers

The aqueous extract of *Aerva lanta* showed significant anti ulcer effect against ulcers induced by cysteamine in a dose dependant manner. Aqueous extract of *Aerva lanata* at a dose of 250 mg/kg showed protective activity of 51.22% and 500mg/kg showed protective activity of 68.27%. Whereas omeprazole showed protective index of 76.10% (table 4).

### Table 4: Effect of Aqueous Extract of *Aerva lanta* In Cysteamine Induced Gastric Ulcers

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Ulcer Index</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Control</td>
<td>12.26±0.27</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td><em>Aerva lanta</em> (250mg/kg)</td>
<td>5.98±0.16</td>
<td>51.22</td>
</tr>
<tr>
<td>III</td>
<td><em>Aerva lanta</em> (500mg/kg)</td>
<td>3.89 ±0.47</td>
<td>68.27</td>
</tr>
<tr>
<td>IV</td>
<td>Omeprazole (20mg/kg)</td>
<td>2.93±0.19</td>
<td>76.10</td>
</tr>
</tbody>
</table>
DISCUSSION

Most of the studies demonstrate the importance of natural products in drug discovery. Keeping this view, we have attempted to study the anti ulcer effect of Aerva lanta aqueous extract was tested against ulcers induced by ethanol, pyloric ligation, indomethacin and cysteamine. Earlier work on Aerva lanta leaves showed significant anti ulcer activity, GC-MS Studies on Aerva lanata by Yamunadevi et al.; revealed the presence of 23 new active compounds [21].

Ethanol has been reported to cause disturbances in gastric secretion, damage to the mucosa, alterations in the permeability, gastric mucus depletion and free radical production. This is attributed to the release of super oxide anion and hydro peroxy free radicals during metabolism of ethanol. oxygen derived free radicals has been found to be involved in the mechanism of acute and chronic ulceration int he gastric mucosa [22], both the doses of Aerva lanta (250 and 500 mg /kg ) were effective in preventing development of ethanol induced gastric ulcer, indicating that Aerva lanta possess gastric cytoprotective effect via antioxidant effects.

Pylorus ligation causes accumulation of gastric acid in the stomach. This increased gastric acid secretion which in turn caused increase in gastric volume, low ph, increased free and total acidity resulting into increase in ulcer index [15, 23]. The lesions produced by this method are located in the lumen region of the stomach. The Aerva lanta extract and omeprazole significantly decreased the total acidity and free acidity; this suggests that it might be having an anti secretory effect.

In order to probe the effectiveness of Aerva lanta extracts in preventing gastric ulcer and their anti secretory effect they were tested against indomethacin induced ulcer. Indomethacin produces erosions and ulcer in the stomach due to the inhibition of prostaglandin synthesis. It also causes cyto destruction of gastric mucosa, disrupts the mucosal blood flow and suppresses gastro duodenal bicarbonate secretion [24, 25]. It can be observed that Aerva lanta in all doses showed significant decrease in ulcer index, (table3) in a dose dependent manner. The protective effect of Aerva lanta could be due to stimulation of prostaglandin secretion in gastric mucosa. Aerva lanta stem also has antioxidant properties, it suggest that Aerva lanta may exert antiulcer activity through scavenging reactive oxygen species [26].

Cysteamine induced duodenal ulcer was characterized by inflammatory changes and hemorrhagic spots occur due to increased gastrin level and gastric acid secretion [27,28] . Pretreatment with extract of Aerva lanta produced significant decrease in the hemorrhagic spots and gastric mucosal damages induced by the cysteamine compared with control group.

CONCLUSION

Our results revealed that aqueous extract of Aerva lanta stem shows significant anti-ulcer activity in gastric mucosal lesions caused by ethanol, pyloric ligation, indomethacin and cysteamine. The results indicate that Aerva lanta extract produced antiulcerogenic effects possessing antisecretory, cytoprotective and anti oxidant mechanism. Further research might explore its exact mechanism of action which is underway.

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