Antiulcerogenic effect on the ethanol extract of the Fruits of *Garcinia mangostana* on Experimental Gastric Ulcer in Rats

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ABSTRACT:
In the ethanol-induced ulcer protocol, *Garcinia mangostana* crude extract (250 and 500 mg/kg) significantly reduced the lesion index, the total lesion area and the percentage of lesion, in comparison with control group. In indomethacin-induced ulcer only the treatments with 500 mg/kg of *Garcinia mangostana* extract and 100 mg/kg of cimetidine reduced significantly in comparison with control group (p < 0.05). Regarding the stress-induced ulcer protocol, it was observed a significant reduction (p < 0.05) in lesion index, total lesion area and in the percentage of lesion in animals treated with *Garcinia mangostana* crude extract (250 and 500 mg/kg) and cimetidine (100 mg/kg). In the gastric secretion determination model, using ligated pylorus, the treatment with *Garcinia mangostana* crude extract (250 and 500 mg/kg) and cimetidine (100 mg/kg), respectively, reduced the volume of gastric juice, total acidity and raised gastric pH appreciably.

Keywords: lesion index, indomethacine, lesion area, cimetidine

INTRODUCTION
The Purple Mangosteen (*Garcinia mangostana*), colloquially known simply as "the mangosteen", is a tropical evergreen tree. The tree grows from 7 to 25 m (20–80 ft) tall. The rind (exocarp) of the edible fruit is deep reddish purple when ripe. Botanically an aril, the fragrant edible flesh can be described as sweet and tangy, citrusy with peach flavor and texture. The Purple Mangosteen belongs to the same genus as the other — less widely known — mangosteens, such as the Button Mangosteen (*G. prainiana*) or the Lemondrop Mangosteen (*G. madruno*).

MATERIALS AND METHODS
Preparation of *Garcinia mangostana* extract
*Garcinia mangostana* samples were collected from Nilgiri hills, Southern India in June 2009. Samples were air-dried at 40 °C for 48 h. The dried fruits of *Garcinia mangostana* was kept in a freezer overnight, powdered (100 g) and submitted to ethanolic extraction (70% ethanol) at room temperature by maceration. After filtration, the extract was concentrated under reduced pressure, yielding 5.2 g of crude *Garcinia mangostana* extract.

Animals
Healthy Female Wister albino rats weighing 150-200g for acute toxicity study and for antiulcer studies, obtained from the animal house of Govt. veterinary college, Pantnagar, (Protocol no. 236/2007) were used in the Present study. All animals were housed in standard propylene cages and fed with standard chow diet (Hindustan Liver, Kolkata) and water *ad libitum* for 2 days before the experiment, maintained with light/dark cycle of 12/12 hours in the temperature 25±2°C. Rats were starved for overnight & was allowed fresh water before administration of the plant extract.

Pharmacological assays
Ethanol-induced ulcer
The experiment was performed according to the method of Morimoto et al. (1991). After 12 h of fasting, rats were randomly divided into four groups of six animals each. To the first group it was given 1 mL of vehicle (1% Tween-80 aqueous solution), and the second group was treated with omeprazole (30 mg/kg). The remaining two groups received 250 and 500 mg/kg of *Garcinia mangostana* crude extract, respectively. All treatments were administered orally. One hour after treatment, all rats received 1 mL of 99.5% ethanol to induce gastric ulcer. After 1 h the animals were sacrificed by cervical dislocation, the stomachs were removed and opened along the greater curvature. Stomachs were gently rinsed with water to remove gastric contents and blood clots before scanning. The obtained images were analyzed by software “EARP” for measuring each lesion point. The ulcers were classified as level I, ulcer area <1 mm²; level II, ulcer area 1–3 mm²; level III, ulcer area >3 mm². The following parameters were determined: (i) Ulcerative Lesion Index (ULI) as 1 × (number of ulcers level I) + 2 × (number of ulcers level II) + 3 × (number of ulcers level III); (ii) curative ratio, which was determined as follow: %C = 100 – (IUtreated × 100/ IUcontrol); (iii) total area of lesion; (iv) percentage of lesion area in relation to the

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total stomach area.

Nonsteroidal anti-inflammatory Garcinia mangostana Linn (NSAID)-induced ulcer

The experiment was performed according to the method of Nwafor et al. (2000). After 12 h of fasting, rats were randomly divided into four groups of six animals each. To the first group it was given 1 mL of vehicle (1% Tween-80 aqueous solution), and the second group was treated with cimetidine (100 mg/kg). The remaining two groups received 250 and 500 mg/kg of Garcinia mangostana crude extract, respectively. All treatments were administered orally. One hour after treatment, all rats received indomethacin (100 mg/kg) to induce gastric ulcer. Four hours later the animals were sacrificed by cervical dislocation, and the abdomen was opened to place another ligature at the oesophageal end. The stomachs were removed and the gastric content was collected and centrifuged at 3000 rpm (8000 × g, 25 °C, 10 min). The amount of gastric-juice acid (mL) and the pH values were determined. Total acid secretion was determined in the supernatant volume by titration to pH 7 using a 0.01 mol⁻¹ NaOH solution, and phenolphthalein as indicator.

RESULTS

In the ethanol-induced ulcer protocol, it was observed that the treatment with Garcinia mangostana crude extract (250 and 500 mg/kg) and omeprazole (30 mg/kg) significantly reduced the lesion index, the total lesion area and the percentage of lesion, in comparison with control group (p < 0.05). On the other hand the indomethacin-induced ulcer protocol, only the treatments with 500 mg/kg of Garcinia mangostana extract and 100 mg/kg of cimetidine reduced significantly all the evaluated parameters in comparison with control group (p < 0.05). Regarding the stress-induced ulcer protocol, it was observed a significant reduction (p < 0.05) in lesion index, total lesion area and in the percentage of lesion in animals treated with Garcinia mangostana crude extract (250 and 500 mg/kg) and cimetidine (100 mg/kg), respectively (Table 1). In the gastric secretion determination model, using ligated pylorus, the treatment with Garcinia mangostana crude extract (250 and 500 mg/kg) and cimetidine (100 mg/kg), respectively, reduced the volume of gastric juice, total acidity and raised gastric pH appreciably (p < 0.05) in comparison with control group (Table 2).

Table 1: Effects of Garcinia mangostana extract (GME) on ethanol, indomethacin and stress-induced gastric ulcers in rats

<table>
<thead>
<tr>
<th>Method</th>
<th>Treatment</th>
<th>Dose (mg/kg)</th>
<th>Total lesion area of % of lesion area</th>
<th>Ulcer index</th>
<th>Inhibition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethanol induced ulcer</strong></td>
<td>Control</td>
<td>—</td>
<td>223.24 ± 26.14</td>
<td>31.24 ± 4.06</td>
<td>48.46 ± 5.87</td>
</tr>
<tr>
<td></td>
<td>Omeprazole</td>
<td>30</td>
<td>0.81 ± 0.81*</td>
<td>0.11 ± 0.23*</td>
<td>0.80 ± 1.02*</td>
</tr>
<tr>
<td></td>
<td>GME</td>
<td>250</td>
<td>7.21 ± 0.87*</td>
<td>2.11 ± 0.63*</td>
<td>11.05 ± 1.12*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500</td>
<td>3.72 ± 2.47*</td>
<td>0.58 ± 0.36*</td>
<td>5.62 ± 3.29*</td>
</tr>
<tr>
<td><strong>Indomethacin induce ulcer</strong></td>
<td>Control</td>
<td>—</td>
<td>32.06 ± 5.32</td>
<td>5.30 ± 0.52</td>
<td>43.12 ± 3.41</td>
</tr>
<tr>
<td></td>
<td>Cimetidine</td>
<td>100</td>
<td>13.45 ± 4.33*</td>
<td>2.35 ± 0.78*</td>
<td>21.37 ± 5.81*</td>
</tr>
<tr>
<td></td>
<td>GME</td>
<td>250</td>
<td>30.27 ± 5.35</td>
<td>3.85 ± 0.75</td>
<td>38.99 ± 6.81</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500</td>
<td>10.35 ± 5.64*</td>
<td>1.73 ± 0.98*</td>
<td>18.40 ± 6.29*</td>
</tr>
<tr>
<td><strong>Stress Induce ulcer</strong></td>
<td>Control</td>
<td>—</td>
<td>132.11±9.77</td>
<td>16.01±1.14</td>
<td>91.90±2.54</td>
</tr>
<tr>
<td></td>
<td>Cimetidine</td>
<td>100</td>
<td>21.57±2.96*</td>
<td>2.46±0.30</td>
<td>24.80±3.26</td>
</tr>
<tr>
<td></td>
<td>GME</td>
<td>250</td>
<td>70.05±9.18*</td>
<td>7.22±0.66</td>
<td>52.38±4.37</td>
</tr>
<tr>
<td></td>
<td></td>
<td>500</td>
<td>34.54±8.75*</td>
<td>3.78±1.06</td>
<td>27.65±2.74</td>
</tr>
</tbody>
</table>

Results are mean ± S.E.M. for six rats. Statistical comparison was performed using ANOVA followed by Dunnet’s test. *p < 0.05 when compared to control group.
pylorus ligature technique revealed that enhance gastric mucosal defensive factors. Moreover, the indicated that gastroduodenal protection by suppress prostaglandin synthesis. Several studies have the ability to cause gastroduodenal ulceration, and (NSAIDs) such as indomethacin mangostana Linn ulcer. Nonsteroidal anti-inflammatory agents, such as ethanol, has been reported to involve the depression of these gastric defensive mechanisms. On one hand, ethanol administration reduces mucus production, gastric mucosal blood flow, bicarbonate secretion, endogenous glutathione and prostaglandin (PG) levels, and on the other hand it increases the release of histamine, the influx of calcium ions, the generation of free radicals and the production of leukotrienes. The formation of gastric mucosal lesions by necrotizing agents, such as ethanol, can be attributed to a number of factors that have been generally referred as mucosal defense. The formation of gastric mucosal lesions by necrotizing agents, such as ethanol, can be attributed to a number of factors that have been generally referred as mucosal defense.

Table 2: Effects of Garcinia mangostana extract (GME) and cimetidine, administered intraduodenally, on the biochemical parameters of gastric juice obtained from pylorus-ligature in rats

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Dose (mg/kg)</th>
<th>Volume (mL)</th>
<th>pH</th>
<th>$[\text{H}^+]$ (mEq/L/4h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>—</td>
<td>2.87±0.50</td>
<td>2.05±0.27</td>
<td>96.69±10.67</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>100</td>
<td>0.72±0.06*</td>
<td>6.14±1.07*</td>
<td>24.21±2.71*</td>
</tr>
<tr>
<td>GME</td>
<td>250</td>
<td>1.06±0.24*</td>
<td>2.43±0.16*</td>
<td>49.97±4.89*</td>
</tr>
<tr>
<td></td>
<td>500</td>
<td>0.82±0.15*</td>
<td>3.09±0.36</td>
<td>49.65±5.84*</td>
</tr>
</tbody>
</table>

Results are mean ± S.E.M. for six rats. Statistical comparison was performed using ANOVA followed by Dunnet’s test. *p ≤ 0.05 when compared to control group.

DISCUSSION

Based on the obtained results it is suggested that Garcinia mangostana extract could prevent gastric lesions caused by ethanol, indomethacin, as well as by stress. These are the most commonly used protocols for the evaluation of anti-ulcer agents in rats. The ability of the gastric mucosa to resist injury by endogenous secretions (acid, pepsin, and bile) and by ingested irritants (e.g. alcohol) can be attributed to a number of factors that have been generally referred as mucosal defense. The formation of gastric mucosal lesions by necrotizing agents, such as ethanol, has been reported to involve the depression of these gastric defensive mechanisms. On one hand, ethanol administration reduces mucus production, gastric mucosal blood flow, bicarbonate secretion, endogenous glutathione and prostaglandin (PG) levels, and on the other hand it increases the release of histamine, the influx of calcium ions, the generation of free radicals and the production of leukotrienes. The formation of gastric mucosal lesions by necrotizing agents, such as ethanol, can be attributed to a number of factors that have been generally referred as mucosal defense.

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