ROLE OF AMARANTHUS SPINOSUS LINN. IN INDOMETHACIN INDUCED GASTRIC ULCER IN RATS

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ABSTRACT
Role of Amaranthus spinosus Linn. in indomethacin induced gastric ulcers was studied in rats. Amaranthus spinosus Linn. Leaves significantly reduced ulcer index induced by indomethacin. The plant leaves produced gastric anti secretory effect by decreasing gastric volume and acidity. It further increased gastric mucin which showed gastric cytoprotective effect. The plant prevented the increased lipid peroxidation during ulceration by indomethacin. Activities of the anti oxidant enzymes were enhanced during ulceration by this plant leaves. Results were comparable to that of ranitidine, a standard anti ulcer drug. Anti ulcerogenic activity of Amaranthus spinosus Linn. leaves was, thus, mediated through anti oxidant defense mechanism.

Keywords: Amaranthus spinosus Linn, indomethacin, ranitidine, gastric ulcer, SOD, CAT, GSH.

INTRODUCTION
Amaranthus spinosus Linn., a medicinal plant under the family of amaranthaceae, is distributed in lower to middle hills (3000–5000 ft) of entire north eastern Himalayas. The plant grows in cultivated areas as well as in waste places. Leaves of Amaranthus spinosus Linn. are stacked and alternate. The plant is known as “prickly amaranthus” in English and “ban lure” or “dhutighans” in Nepali. Medicinal uses of Amaranthus spinosus Linn. as
mentioned in Ayurvedic text[1,2] are: Leaf infusion is diuretic and used in anemia. Root paste is used in gonorrhea, eczema, menorrhea etc. Ethnic use of *Amaranthus spinosus* Linn. is mainly with village-people of Sikkim who use leaf infusion of the plant in stomach disorder specially in case of indigestion and peptic ulcer [3].

Recently we observed anti ulcer activity of the leaves of *Amaranthus spinosus* Linn. against ethanol induced gastric ulcer in albino rats[4]. Tempted by this observation we undertook studies to note role of *Amaranthus spinosus* Linn. against indomethacin induced gastric ulcer in rats. In present communication effect of *Amaranthus spinosus* Linn. leaves on indomethacin induced gastric ulcer in albino rats and the possible mechanism involved therein are being reported.

**MATERIAL AND METHODS**

**Plant material**

![Amaranthus spinosus Linn.](image)

Leaves of *Amaranthus spinosus* Linn. were collected from the medicinal plants garden of the University of North Bengal during August – September, 2013 and authenticated by the taxonomist of the department of Botany of the said University. A voucher specimen was kept in the department for future reference. Leaves were shed dried and powdered. The powder was used as the test drug.

**Preparation of the Test Drug**

Leaves of *Amaranthus spinosus* Linn. were shed dried and powdered. The powder was used as the test drug.

**Experimental animals**

Wistar strain albino rats (150 - 180 g) of either sex were used for the study. Rats were
housed in colony cages (5 rats / cage) and were kept for at least a week in the experimental wing of the animal house (room temperature 25 – 28 degree centigrade and humidity 60 – 65% with 12 h light and dark cycle) before experimentation. Animals were fed on laboratory diet with water ad libitum. 8 rats were used for each set of experiment. The animal experiment was approved by the ethics committee of the Institute.

**Chemicals and Drugs**
All chemicals used in this experiment were procured from Ranbaxy and SD Fine Chemicals, New Delhi, India. Indomethacin (Torrent Research Centre, Gandhinagar), ranitidine (Cipla pharmaceuticals) were used in the study.

**Acute toxicity study**
Acute toxicity study of *Amaranthus spinosus* Linn. was done by the method of Ghosh[5]. Rats were starved overnight (water is supplied ad libitum) and were divided into five groups of ten each. Powdered leaves of *Amaranthus spinosus* Linn. was given to the rats orally through feeding tube in increasing dose levels of 0.1, 0.5, 1, 3 and 5g/kg body weight. The animals were observed continuously for 2 hours for the following:

- **a) Behavioral profile**: alertness, restlessness, irritability and fearfulness.
- **b) Neurological profile**: spontaneous activity, reactivity, touches response, pain response and gait.
- **c) Autonomic profile**: defecation and urination.

The number of deaths, if any, was recorded after 24 and 72 hours.

**Production of gastric ulcer**
Indomethacin induced gastric ulcer was produced by the method of Parmar and Desai [6] with slight modification. Rats were fasted for 18 h when no food but water was supplied ad libitum. Indomethacin(10 mg/kg) was given to rats orally through a feeding tube in two doses at an interval of 15 hour. 1h after administration of last dose, pylorus part of the animals was ligated. Four hours after the pyloric ligation the animals were sacrificed by cervical dislocation. The stomach was taken out, gastric juice collected and the stomach was then incised along the greater curvature to examine the ulcers.

**Antiulcer Study**
Rats were divided into 4 groups.
1. Control: Rats took normal diet and water.
2. Indomethacin treated: Rats were treated with indomethacin.
3. Indomethacin + *Amaranthus spinosus* Linn.: Powdered leaves of *Amaranthus spinosus* Linn. was given to the rats orally through feeding tube 30 minutes prior to each dose of indomethacin.
4. Indomethacin + Ranitidine: Ranitidine was given in the dose of 50 mg/kg p.o. 30 minutes before each dose of indomethacin. Dose of ranitidine was selected based on the report of Khare *et al.* [7]

**Evaluation of Ulcer Index**

This was done by the method of Szelenyi and Thiemer, [8]. Gastric lesions were counted and the mean ulcerative index was calculated as follows:

I – Presence of edema, hyperemia and single sub mucosal punctiform hemorrhage.

II – Presence of sub mucosal hemorrhagic lesions with small erosions.

III – Presence of deep ulcer with erosions and invasive lesions.

Ulcer index = (number of lesion I) x 1 + (number of lesion II) x 2 + (number of lesion III) x 3.

**Biochemical estimations**

Collected gastric juice from the rat’s stomach was centrifuged and its volume and pH were measured. Gastric juice was further used for the estimation of free and total acidity as described by Hawk *et al.*[9], pepsin content by the method of Anson [10], mucin by our method [11] and total protein by the method of Lowry *et al.*[12].

The mucosal tissue from rat’s stomach was scrapped and then homogenized (5%) in ice cold 0.99% saline with a Potter – Elvehjem glass homogenizer for 30 sec. The homogenate was used for the estimations of DNA [13], nitric oxide [14], lipid peroxides [15], superoxide dismutase [16], catalase [17], glutathione [18], and glutathione peroxidase [19].

**Statistical Analysis**

The values were expressed as mean ± SEM and were analyzed using one-way analysis of variance (ANOVA) using Statistical Package for Social Sciences (SPSS) 20th versions. Differences between means were tested employing Duncan’s multiple comparison test and significance was set at p < 0.05.
RESULTS AND DISCUSSION

Effect of powdered leaves of *Amaranthus spinosus* Linn. on acute toxicity study
Acute toxicity studies revealed the non toxic nature of powdered leaves of *Amaranthus spinosus* Linn. No toxic reactions were found in any one of the selected doses till the end of the study. All rats were healthy and active during the experimental period. Not a single rat died during the study.

Effect of *Amaranthus spinosus* Linn on indomethacin induced gastric ulcers in rats
Results relating to effects of *Amaranthus spinosus* Linn. and ranitidine against indomethacin induced gastric ulcer in rats were shown in Table -1.

Indomethacin produced massive ulcers in glandular part of rat’s stomach. Incidence of ulceration was 100%. Acute dilatation and hemorrhage were seen in stomach. In one rat perforation of the stomach was noted. Ulcer index came 30.8 ± 1.32. Pretreatment of rats with *Amaranthus spinosus* Linn. leaves gave significant protection (26.62%, 65.58% and 65.91% by the doses 0.5 g/kg, 1.0 g/kg and 1.5 g/kg respectively) to the animals from forming ulcers by indomethacin. Ranitidine (50 mg/kg), however, gave 71.43% protection.

Effect of *Amaranthus spinosus* Linn. leaves on volume and pH of gastric juice during indomethacin induced gastric ulcer in rats.
Results were shown in Table – 2. Indomethacin increased volume of gastric juice and decreased its pH in rats. In control rats volume and pH of gastric juice were 1.22 ± 0.05 and 2.98 ± 0.07 respectively. In indomethacin group the same values came 3.34 ± 0.08 and 1.71 ± 0.06 respectively. Changes were statistically significant (p<0.001). Pretreatment of rats with *Amaranthus spinosus* Linn. leaves, however, could decrease volume of gastric juice (1.32 ± 0.07) and increase its pH (2.73 ± 0.05). Effects were comparable to that of ranitidine.

Effect of *Amaranthus spinosus* Linn. leaves on free and total acidity of gastric juice during indomethacin induced gastric ulcer in rats.
Table – 3 showed effects of *Amaranthus spinosus* Linn. leaves and ranitidine on free and total acidity of gastric juice during indomethacin induced gastric ulcer in rats. Indomethacin significantly increased both free and total gastric acidity. Free and total gastric acidity of control rats were 10.22 ± 0.48 and 30.22 ± 0.48 respectively. For indomethacin group values came 22.79 ± 1.22 (free acidity) and 75.78 ± 2.86 (total acidity).
Acidity. *Amaranthus spinosus* Linn. leaves could decrease free and total gastric acidity (13.18 ± 0.61 and 48.35 ± 1.45 respectively). Ranitidine also decreased raised free and total gastric acidity during indomethacin induced gastric ulcers.

**Effect of *Amaranthus spinosus* Linn. leaves on gastric pepsin and mucin during indomethacin induced gastric ulcer in rats.**

Effects of *Amaranthus spinosus* Linn. and ranitidine on gastric pepsin and mucin during indomethacin induced gastric ulcer in rats were shown in Table - 4. It appears from the table that indomethacin elevated activity of gastric pepsin (44.38 ± 1.58, control - 30.81 ± 1.08) and lowered mucin content of gastric juice (1.68 ± 0.13, control - 5.27 ± 0.33). Changes were statistically significant (p<0.001). *Amaranthus spinosus* Linn. could decrease gastric pepsin activity and increase mucin content of gastric juice during indomethacin induced gastric ulcer in albino rats. Results were comparable to that of ranitidine.

**Table-1. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on indomethacin (INDO) induced gastric ulcer in albino rats.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Ulcer index (mean ± SEM)</th>
<th>% Ulcer protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Nil</td>
<td>--</td>
</tr>
<tr>
<td>INDO</td>
<td>30.8 ± 1.32</td>
<td>--</td>
</tr>
<tr>
<td>INDO+ ASL (0.5 g/kg)</td>
<td>22.6 ± 1.13*</td>
<td>26.62</td>
</tr>
<tr>
<td>INDO+ ASL (1.0 g/kg)</td>
<td>10.6 ± 1.19**</td>
<td>65.58</td>
</tr>
<tr>
<td>INDO+ ASL (1.5 g/kg)</td>
<td>10.5 ± 1.11**</td>
<td>65.91</td>
</tr>
<tr>
<td>INDO+ Ranitidine (50mg/kg)</td>
<td>8.8 ± 1.01**</td>
<td>71.43</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, *p<0.05, **p<0.001

**Table-2. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on volume and pH of gastric juice during indomethacin (INDO) induced gastric ulcer in albino rats.**

<table>
<thead>
<tr>
<th>Group</th>
<th>Volume of gastric juice (ml)</th>
<th>pH of gastric juice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.22 ± 0.05</td>
<td>2.98 ± 0.07</td>
</tr>
<tr>
<td>INDO</td>
<td>3.34 ± 0.08**</td>
<td>1.71 ± 0.06**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>1.32 ± 0.07**</td>
<td>2.73 ±0.05**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>1.29 ± 0.06**</td>
<td>2.88 ± 0.06**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, **p<0.001
Table-3. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on free and total gastric acidity during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Free acidity (mEq/l/100g)</th>
<th>Total acidity (mEq/l/100g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>10.22 ± 0.48</td>
<td>30.22 ± 0.48</td>
</tr>
<tr>
<td>INDO</td>
<td>22.79 ± 1.22**</td>
<td>75.78 ± 2.86**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>13.18 ± 0.61**</td>
<td>48.35 ± 1.45**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>10.85 ± 0.56**</td>
<td>33.83 ± 1.16**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001

Table-4. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on gastric pepsin and mucin content during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Pepsin (micromole/ml)</th>
<th>Mucin (microgram/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>30.81 ± 1.08</td>
<td>5.27 ± 0.33</td>
</tr>
<tr>
<td>INDO</td>
<td>44.38 ± 1.58**</td>
<td>1.68 ± 0.13**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>31.87 ± 1.13**</td>
<td>4.78 ± 0.21**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>33.79 ± 1.59**</td>
<td>4.52 ± 0.11**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001

Table-5. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on gastric protein and DNA content during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Protein (mg/ml)</th>
<th>DNA (microgram/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>35.11 ± 1.58</td>
<td>135.11 ± 5.18</td>
</tr>
<tr>
<td>INDO</td>
<td>10.25 ± 1.13**</td>
<td>85.12 ± 3.22**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>29.33 ± 1.11**</td>
<td>120.78 ± 0.021**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>32.23 ± 1.71**</td>
<td>128.31 ± 4.33**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001

Table-6. Effect of *Amaranthus spinosus* Linn. leaves (ASL) on gastric nitric oxide and lipid peroxides during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Nitric oxide (micromole/g wet tissue)</th>
<th>Lipid peroxides (nm/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>115.11 ± 7.92</td>
<td>4.28 ± 0.04</td>
</tr>
<tr>
<td>INDO</td>
<td>190.34 ± 8.16**</td>
<td>9.56 ± 0.07**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>128.78 ± 7.82**</td>
<td>4.88 ± 0.07**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>120.31 ± 6.71**</td>
<td>4.52 ± 0.05**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001
Table-7. Effect of *Amaranthusspinosus* Linn. leaves (ASL) on superoxide dismutase and catalase activity during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Superoxide dismutase (SOD) (Unit/g wet tissue)</th>
<th>Catalase (CAT) (Unit/g wet tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>134.75 ± 5.13</td>
<td>24.21 ± 2.05</td>
</tr>
<tr>
<td>INDO</td>
<td>88.65 ± 2.01**</td>
<td>9.11 ± 1.16**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>120.11 ± 4.01**</td>
<td>18.34 ± 2.04**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>128.51 ± 4.06**</td>
<td>20.31 ± 2.01**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001

Table-8. Effect of *Amaranthusspinosus* Linn. leaves (ASL) on glutathione and Glutathione per oxidase activity during indomethacin (INDO) induced gastric ulcer in albino rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Glutathione (GSH) (micro mole/mg protein)</th>
<th>Glutathione per oxidase (Micro mole of GSH consumed/min/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.88 ± 0.09</td>
<td>234.72 ± 7.14</td>
</tr>
<tr>
<td>INDO</td>
<td>1.52 ± 0.05**</td>
<td>189.51 ± 5.02**</td>
</tr>
<tr>
<td>INDO + ASL (1.0 g/kg)</td>
<td>4.47 ± 0.06**</td>
<td>214.34 ± 6.01**</td>
</tr>
<tr>
<td>INDO + Ranitidine (50mg/kg)</td>
<td>4.62 ± 0.05**</td>
<td>225.82 ± 6.01**</td>
</tr>
</tbody>
</table>

Results were in mean ± SEM, Each group had eight rats, ** p<0.001

Effect of *Amaranthusspinosus* Linn. leaves on gastric protein and DNA content of gastric mucosa during indomethacin induced gastric ulcer in rats.

Results are given in Table – 5. Gastric protein and DNA content of gastric mucosa were found to be decreased by indomethacin. Values were statistically significant (p<0.001). Pretreated group of rats by *Amaranthusspinosus* Linn. leaves showed increased values of gastric protein and DNA content of gastric mucosa which were more close to the normal values. Results were comparable to that of ranitidine.

Effect of *Amaranthusspinosus* Linn. leaves on gastric nitric oxide and lipid peroxides during indomethacin induced gastric ulcer in rats.

Nitric oxide levels and lipid peroxides were increased significantly (p<0.001) in indomethacin treated rats. Pretreatment with *Amaranthusspinosus* Linn. leaves reversed this enhanced free radicals. Values came down almost to controls. Ranitidine also decreased nitric oxide levels and lipid peroxides during indomethacin induced gastric ulcers. Results are shown in Table – 6.
Effect of *Amaranthus spinosus* Linn. Leaves on gastric superoxide dismutase and catalase activity during indomethacin induced gastric ulcer in rats.

Gastric superoxide dismutase and catalase activity was found significantly decreased during indomethacin induced gastric ulcer. But in group of rats pretreated with *Amaranthus spinosus* Linn. leaves activities of these enzymes were maintained near normal. Same trend was also noticed for ranitidine (Table – 7).

Effect of *Amaranthus spinosus* Linn. Leaves on gastric glutathione and glutathione peroxidase activity during indomethacin induced gastric ulcer in rats.

Results are given in Table – 8. Indomethacin caused significant decrease in gastric glutathione level and glutathione peroxidase activity. Rats pretreated with *Amaranthus spinosus* Linn. leaves showed increased glutathione level and glutathione peroxidase activity in indomethacin group and the values were near to control values.

The term “Peptic ulcer” refers to an ulcer in the lower oesophagus, stomach or duodenum, in the jejunum after surgical anastomosis to the stomach or, rarely in the ileum adjacent to a Meckel’s diverticulum. Ulcer in the stomach (gastric ulcer) may be acute or chronic. Quincke [20] was probably the first to use the term ‘Peptic ulcer’. Because of its frequency and worldwide distribution, peptic ulcer continues to be a subject of numerous investigations, both experimental and clinico pathological. In this respect peptic ulcer occupies a place secondary to carcinoma in the field of gastroenterology.

There is medicine to treat peptic ulcer [21]. In case, the ulcer is due to infection of *Helicobacter pylori* (*H. pylori*), the different medications are usually prescribed. This is known as “Triple therapy”. This includes a proton pump inhibitor viz. omeprazole to reduce acid production and two antibiotics to get rid of the organism. Sometimes, instead of one of the antibiotics, bismuth salicylate may be the third medication recommended. This drug, available over the counter, coats and soothes the stomach, protecting it from the damaging effects of acid. Two, rather than three, drug regimens are currently being developed. For non *H. pylori* ulcers number of drugs are now available for treatment. These drugs are broadly classified into two categories:

1) Those that decrease or counter acid – pepsin secretion viz. ranitidine, famotidine etc. (*H2 - blockers*), pirenzepine, telenzepine etc. (*M1 – blockers*), omeprazole, lansaprazole etc. (*proton pump inhibitors*).
2) Those that affect cytoprotection by virtue of their effects in mucosal defense factors like sucralfate, carbenoxolone etc. [22]

No doubt the above said drugs have brought about remarkable changes in peptic ulcer therapy, the efficacy of these drugs is still debatable. Reports on clinical evaluation of these drugs show that there are incidences of relapses and adverse effects and danger of drug interactions during ulcer therapy. Hence, the search for an ideal anti-ulcer drug continues and has also been extended to medicinal plants/herbs in search for new and novel molecules, which afford better protection and decrease the incidence of relapse.

Numerous medicinal plants showed anti gastric ulcer activity. Sanyal et al. [23] found that vegetable banana is efficacious not only for experimentally induced gastric ulcers in albino rats, guinea pigs etc. but also for human being suffering from gastric ulcers. Akahet et al. [24] demonstrated anti gastric ulcer activity of the herb Cassampelosmucronata. Likewise Shetty et al. [25], Sairamet al. [26], Maity et al. [27,28] and Dharmani and Palit [29] confirmed anti gastric ulcer activities of Ginkgo biloba, Convolvulus pluricaulis Choisy, tea root extract and Vernonialasiopous respectively. We also reported anti gastric ulcer activities of few medicinal plants in different experimental ulcer models [30-35].

*Amaranthusspinosus* Linn., a plant of Eastern Himalaya, was known for its ethnic use in peptic ulcer [3]. In screening programme we noted anti gastric ulcer activity of *Amaranthusspinosus* Linn. [33] Hussain et al. [36] showed that ethanol extract of whole plant of *Amaranthusspinosus* Linn. has anti diarrheal and anti ulcer activity in experimental animals. Recently we noticed anti ulcer activity of *Amaranthusspinosus* Linn.in ethanol induced gastric ulcer and cysteamine induced duodenal ulcer in albino rats [4]. Since experiments with more gastric ulcer models are needed to confirm anti gastric ulcer activity of a material we studied effect of *Amaranthusspinosus* Linn.plants on indomethacin induced gastric ulcer in rats and the possible mechanism involved therein.

Results showed that *Amaranthusspinosus* Linn.leaves could prevent formation of indomethacin induced gastric ulcer by 65.58%. The result was comparable to that of Ranitidine, the standard drug of ulcer, where inhibition rate was 71.43% (Table – 1).
In ulcer research emphasis has been given on rate of gastric secretion and gastric pH[37]. Indomethacin increased gastric secretion in rats. *Amaranthus spinosus* Linn. leaves could lower the increased gastric secretion to almost normal level. This gastric inhibitory activity of the plant, perhaps, helps to prevent formation of gastric ulcer by indomethacin. The plant leaves also increased pH of gastric juice (Table – 2).

Elevated gastric acidity is responsible for ulcer formation [20]. Indomethacin increased gastric free and total acidity. Gastric acidity of rats pretreated with *Amaranthus spinosus* Linn. leaves showed more or less normal values. This helps to prevent ulcer formation by indomethacin. Ranitidine also decreased gastric acidity (Table – 3).

Pepsin has relation with development of gastric ulcer. In many cases of gastric ulcers, gastric pepsin was found elevated[21]. The present study showed that gastric pepsin was elevated during indomethacin induced gastric ulcer which came to almost normal level by the pretreatment with *Amaranthus spinosus* Linn. leaves. Gastric mucin which gives cyto protection to stomach[38] was found decreased by indomethacin and reversed back to control level by pretreatment with *Amaranthus spinosus* Linn. leaves (Table – 4). This suggests cyto protective activity of the plant.

In experimental ulcers levels of gastric protein and DNA of gastric mucosa are found to be decreased[38]. Indomethacin could develop ulcer by decreasing gastric protein and DNA of gastric mucosa. Rats pretreated with *Amaranthus spinosus* Linn. leaves showed increased amount of these materials and thereby could prevent ulcer formation (Table – 5) Gastric mucosal lipid peroxidation has been reported to increase incidence of experimental ulcers [39]. In this study we noted elevated levels of nitric oxide and lipid peroxides in gastric mucosa during indomethacin induced gastric ulceration. Pretreatment of rats by *Amaranthus spinosus* Linn. leaves could decrease levels of gastric nitric oxide and lipid peroxides thus prevent indomethacin induced ulcer formation (Table – 6).

Free radicals scavenging enzymes like superoxide dismutase, catalase, glutathione per oxidase are involved in development of gastric ulcer. If generation of free radicals exceeds the ability of free radical scavenging enzymes, gastric mucosa may be injured by the free radicals resulting development of gastric ulcer [40]. Activities of all these free radical scavenging enzymes were found decreased by indomethacin which was reversed by pretreatment with *Amaranthus spinosus* Linn. leaves (Tables - 7, 8).
From the results of this study, it may be stated that indomethacin could increase gastric lipid peroxidation therefore generate reactive oxygen metabolites. This could damage gastric cells. This was reflected by decreased amount of DNA in gastric mucosa which, in turn, was responsible for decreased synthesis of gastric mucosubstances. In absence of proper protective layer of mucosubstances, ulcer developed in the stomach. *Amaranthus spinosus* Linn. leaves, on the other hand, could inhibit gastric lipid peroxidation thereby inhibit generation of reactive oxygen metabolites. This could protect the gastric cells from damage. DNA of gastric mucosa was, thus, found increased with concomitant increase in the level of mucosubstances. These mucosubstances gave proper protection in the stomach for which ulcer could not develop.

**CONCLUSION**

Anti ulcerogenic activity of *Amaranthus spinosus* Linn. leaves against indomethacin induced gastric ulcers in rats was mediated through anti oxidant defense mechanism.

**REFERENCES**


