Effect of *Convolvulus pluricaulis* Chois on gastric ulceration and secretion in rats

K Sairam, Ch V Rao & R K Goel*

Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005.

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*Correspondent author: Fax: 0542-367568.
E-mail:rkgoel@banaras.ernet.in

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*Convolvulus pluricaulis* is an indigenous plant commonly mentioned in Ayurveda, an ancient system of Indian medicine, as a rasayana which is mainly advocated for use in rejuvenation therapy. The present study was conducted to evaluate the potential anti-ulcerogenic effect of juice of fresh whole plants of *C. pluricaulis* (CPJ) against various experimental gastric ulcer models induced by ethanol, aspirin, 2 hr cold restraint stress and 4 hr pyloric ligation in rats. The drug was given orally twice daily for five days in the doses of 375 and 750 mg/kg body weight. CPJ showed anti-ulcerogenic effect at both doses in all the experimental gastric ulcer models and was comparable to the reference drug sucralfate (250 mg/kg). Gastric juice secretion and mucosal studies were undertaken to find out the possible mechanism of action of antulcer effect by studying its effects both on offensive and defensive mucosal factors. The antiulcerogenic effect of CPJ was found to be due to augmentation of mucosal defensive factors like mucus secretion, lifespan of mucosal cells and glycoproteins rather than on the offensive factors like acid-pepsin.

*Convolvulus pluricaulis* Chois (CP) is an indigenous hairy perennial native plant of some parts of northern India and Bihar. It has been commonly mentioned as a rasayana in several Ayurvedic texts including *Caraka Samhita* and *Cakradatta*. A rasayana is one which promotes longevity and prevents diseases by providing strength and immunity. In *Caraka Samhita*, it is mentioned as one of the ingredients of Bramha rasayana, which is advocated for use in rejuvenation therapy. The juice of CP mixed with other ingredients is used to alleviate insanity. CP is reported to have and hypnotic activity and is clinically effective in anxiety neurosis.

Precise etiology of ulcer is unclear and a satisfactory regimen still remains elusive. Many factors are thought to be involved in the pathogenesis of ulcer. Ulcers are thought to be due to an imbalance in (a) offensive factors like acid and pepsin and (b) defensive factors like mucin secretion, cell proliferation, prostaglandins etc. Most of the available drugs are thought to act on the offensive factors, such as antacids which neutralize acid secretion and H2 receptor blockers, viz. ranitidine, famotidine etc., anticholinergics like pirenzepine, telezipine etc., and proton pump inhibitors like omeprazole etc., which interfere with acid secretion, whereas sucralfate is cytoprotective drug is also reported to have anti- peptic activity. A number of herbal drugs including banana powder and Tambarabasma, a traditional preparation of copper have been reported to have antiulcer activity by virtue of their beneficial effects on mucosal defensive factors like mucus secretion.

Stress is one of the important factors for gastric ulceration. *CP* being a rasayana akin to the modern adaptogens, which are mostly used for stress related disorders, it was thought prudent to experimentally evaluate the potential anti-ulcer activity of juice of *Convolvulus pluricaulis* (CPJ). Further, studies were done to probe its possible role in offensive and defensive factors involved in ulcerogenesis.

**Materials and Methods**

**Animals**—Albino rats of CF strain of either sex weighing between 150 - 180 g were procured from the Central Animal House of the Institute and were housed in well ventilated colony cages in the departmental animal house at 25°C ± 2°C and 45-55% RH, 10:14 hr L:D cycle for one week for acclimatization. The animals were fed with standard rodent pellet diet (Hind Lever) and water *ad libitum*.

**Collection of plant**—*C. pluricaulis* of cultivated variety was obtained in the month of April from the Ayurvedic gardens of the Institute and was identified with the reference herbarium maintained in the Department of Dravyaguna. Whole green plants (1 kg) were size reduced, crushed and 200 ml of juice thus obtained was filtered. The dry weight in terms of solid content in the juice was 2.5%. The fresh juice...
was stored in a refrigerator at -20°C in a glass containers of 20 ml capacity and was used with in a week of its extraction. The juice was warmed each time at 37°C before administration to the animals.

Experimental study—CPJ in doses of 0.75 and 1.5 ml/100 g (equivalent to 325 and 750 mg/kg, in terms of dry weight) and sucralfate (SF) in the dose of 250 mg/kg were administered orally, twice daily at 1000 and 1600 hrs respectively for 5 days. On the 6th day of experiment, the 18 h fasted rats were subjected to the following experimental gastric ulcer studies:

a) Ethanol (ETH)- induced ulcers: The gastric ulcers were induced in rats by administering orally 100% ETH (1 ml/200 g)11 and the animals were sacrificed by cervical dislocation after 1 hr of ETH administration and stomach was incised along the greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcers present in the glandular portion of the stomach (mm²/rat). Statistical analysis of data was done by using unpaired Student’s t test.

b) Aspirin (ASP)- induced ulcers: ASP in dose of 200 mg/kg (20 mg/ml) was administered to the animals on the day of the experiment and ulcers were scored after 4 hr as described earlier15. The number of ulcers per stomach was noted and the severity of the ulcers was scored after histological confirmation as follows: 0, no ulcer; +, pin point ulcer and histological changes limited to superficial layers of mucosa and no congestion; ++, ulcer size less than 1 mm and half of the mucosal thickness showed necrotic changes; ++++, ulcer size 1-2 mm with more than two-thirds of the mucosal thickness destroyed with marked necrosis and congestion, muscularis remaining unaffected; +++++, ulcer either more than 2 mm in size or perforated with complete destruction of the mucosa with necrosis and haemorrhage, muscularis still remaining unaffected. The pooled group ulcer score was then calculated18. Statistical analysis was done by using Wilcoxon Sum Rank test19.

c) Cold-restraint stress (CRS)- induced ulcers: On day six, cold restraint stress was given to 18 hr fasted rats by strapping the rats on a wooden plank and keeping them at 4°-6°C for 2 hr. The animals were then sacrificed by cervical dislocation and ulcers were scored on the dissected stomachs16 as described above.

d) Pylorus-ligated (PL)- rats: Drugs were administered for a period of 5 days. On day six after the last dose, the rats were kept for 18 hr fasting and care was taken to avoid coprophagye. Animals were anaesthetized using pentobarbitone (35 mg/kg, ip), the abdomen was opened and pyloric ligation was done without causing any damage to its blood supply. The stomach was replaced carefully and the abdomen wall was closed in two layers with interrupted sutures. The animals were deprived of water during the post-operative period17. After 4 hr, stomachs were dissected out and contents were collected into tubes for estimation of biochemical parameters. The stomach was taken out and cut open along the greater curvature and ulcers were scored by a person unaware of the experimental protocol in the glandular portion of the stomach as mentioned in aspirin induced ulcers.

Gastric secretion—The gastric juice was collected 4 hr after PL and centrifuged for 5 min at 2000 rpm and the volume of the supernatant was expressed as ml/100g body weight. Total acid output was determined by titrating with 0.01 N NaOH, using phenolphthalein as indicator and is expressed as μEq/4hr. Peptic activity was determined using haemoglobin as substrate20 and has been expressed as μmol/ml and μmol/4 hr for concentration and output respectively. Dissolved mucosubstances were estimated in the 90% alcoholic precipitate of the gastric juice. The precipitate, thus obtained was either dissolved in 1 ml of 0.1 N NaOH or 1 ml of 0.1 N H2SO4. The former was used for the estimation of protein21, total hexoses22, hexosamine23 and fucose24, while the latter was used for the estimation of sialic acid25. The results are expressed in μg/ml. The ratio of total carbohydrate (TC) (sum of total hexoses, hexosamine, fucose and sialic acid) to protein (P) has been taken as the index of mucin activity26. DNA content were estimated and expressed as μg/ml gastric juice/100g weight of rat27.

Gastric mucosal studies—Samples of gastric mucosa were homogenized in normal saline and treated with 90% ethanol and were subjected for the estimation of carbohydrates and proteins using the methods described above for gastric juice contents. Statistical analysis of data was done by using unpaired Student’s t test.

Results

CPJ in the doses of 375 - 750 mg/kg, twice daily, given for 5 days orally, showed significant protection against various experimental gastric ulcers induced by ethanol, aspirin, 2hr cold restraint stress and 4h pyloric ligation in rats and was comparable to the
reference drug sucralfate (250 mg/ kg, twice daily, orally for 5 days) (Table 1). In gastric secretion studies, CPJ (375 - 750 mg/ kg) did not show any significant effect on volume, concentration and output of acid and pepsin secretion. However, SF showed significant reduction in concentration and output of pepsin (Table 2) with little or no effect on volume and acid secretion. A significant reduction in DNA content of the gastric juice was observed with both the doses of CPJ and SF (Table 2).

Effect of different doses of CPJ and SF on mucin secretion and mucosal glycoproteins is shown in Table 3. On mucin secretion, CPJ at the lower dose produced significant changes in hexosamine and TC:P, whereas the higher dose produced significant increase not only in hexosamine and TC:P but also in levels of other individual carbohydrates like total hexoses and steric acid and total carbohydrates compared to the control group. SF at 250 mg/ kg produced a significant change in steric acid, total carbohydrates and TC:P ratio, while other parameters were not significantly altered.

On mucosal glycoproteins, a significant increase was observed in TC:P ratio with higher dose of CPJ and SF. The significant increase in TC:P was due to their effects on individual carbohydrates and protein content which either tended to increase or decrease respectively, except for a significant increase in steric acid content with SF.

Discussion

The juice of fresh plants of *C. pluricaulis* has been found to possess significant antiulcer activity in various experimental gastric ulcer models and was comparable to the reference drug sucralfate. The protective effect of CPJ on different models may be due to activities covering a wide range, as many factors are thought to be involved in pathogenesis of gastric ulcers in different models. The damage produced by ethanol to gastric mucosa is due a number of contributing factors, which include effects on mucosal blood flow, platelet thrombi, damage to capillary endothelium and release of arachidonate metabolites, specifically LTC₄/D₄ and PAF. NSAIDs produce gastric ulcers by inhibiting formation of PGs, which are essential for integrity of mucosa as they have various mucosal defensive actions. Further PGs increase the conversion of hydroxy fatty acids in the lipoxygenase pathway and xanthone-oxidase activity in the mucosa. PL induced ulcers are

### Table 1—Effect of juice of *C. pluricaulis* (CPJ) on ethanol (ETH, 100%, 1 ml/200 g, po, 1 hr)-, aspirin (ASP, 200 mg/kg, po, 4 hr)-, 2 hr cold restraint stress (CRS)-, and 4 hr pylorus ligated (PL)-induced gastric ulcers in rats.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Ulcer index (ETH mm²/rat)</th>
<th>Protection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>25.3±5.9</td>
<td>—</td>
</tr>
<tr>
<td>CPJ 375</td>
<td>9.0±3.7</td>
<td>64.4</td>
</tr>
<tr>
<td>750</td>
<td>4.3±1.9</td>
<td>83.0</td>
</tr>
<tr>
<td>SF</td>
<td>6.2±1.4</td>
<td>75.5</td>
</tr>
<tr>
<td>Control</td>
<td>17.8±3.3</td>
<td>—</td>
</tr>
<tr>
<td>CPJ 375</td>
<td>11.0±2.6</td>
<td>38.2</td>
</tr>
<tr>
<td>750</td>
<td>6.4±2.2</td>
<td>64.0</td>
</tr>
<tr>
<td>SF 250</td>
<td>4.8±2.5</td>
<td>73.0</td>
</tr>
<tr>
<td>Control</td>
<td>18.9±2.8</td>
<td>—</td>
</tr>
<tr>
<td>CAJ 375</td>
<td>11.0±1.9</td>
<td>41.8</td>
</tr>
<tr>
<td>750</td>
<td>9.3±2.8</td>
<td>50.8</td>
</tr>
<tr>
<td>SF 250</td>
<td>8.2±1.7</td>
<td>56.6</td>
</tr>
<tr>
<td>Control</td>
<td>14.6±3.2</td>
<td>—</td>
</tr>
<tr>
<td>CPJ 375</td>
<td>6.0±2.0</td>
<td>58.9</td>
</tr>
<tr>
<td>750</td>
<td>4.1±1.7</td>
<td>71.9</td>
</tr>
<tr>
<td>SF 250</td>
<td>4.3±1.8</td>
<td>70.5</td>
</tr>
</tbody>
</table>

*P values: *<0.05, *b <0.01

### Table 2—Effect of CPJ on gastric juice volume, acid, pepsin, and DNA contents in 4 hr PL rats.

<table>
<thead>
<tr>
<th>Treatment (mg/kg, bd x 5 days)</th>
<th>Volume (ml/100g)</th>
<th>Acid Concentration (μEq/ml)</th>
<th>Acid Output (μEq/4hr)</th>
<th>Pepsin Concentration (μmol/ml)</th>
<th>Pepsin Output (μmol/4hr)</th>
<th>DNA (μg/ml/100g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.18±0.13</td>
<td>111.6±58.0</td>
<td>137.6±14.0</td>
<td>652.5±58.2</td>
<td>787.4±72.9</td>
<td>273.5±23.2</td>
</tr>
<tr>
<td>CPJ 375</td>
<td>1.39±0.11</td>
<td>98.3±5.4</td>
<td>142.5±17.6</td>
<td>639.5±49.4</td>
<td>893.3±71.5</td>
<td>200.2±20.8</td>
</tr>
<tr>
<td>750</td>
<td>1.16±0.14</td>
<td>89.2±8.7</td>
<td>104.7±16.5</td>
<td>635.4±52.2</td>
<td>747.2±78.9</td>
<td>169.8±27.6</td>
</tr>
<tr>
<td>SF 250</td>
<td>1.12±0.14</td>
<td>96.2±8.4</td>
<td>109.4±10.2</td>
<td>476.1±65.0</td>
<td>535.2±81.3</td>
<td>166.5±22.2</td>
</tr>
</tbody>
</table>

*P values: *<0.05, *b <0.01
thought to be caused due to increased presence of acid and pepsin in the stomach\(^8\). Stress induced ulcers are caused by a number of factors both physical and psychological\(^{30}\). Increase in gastric motility\(^{31}\), vagal overactivity\(^{32}\), mast cell degranulation\(^{33}\), decreased gastric mucosal blood flow\(^{34}\) and decreased gastric muscular blood flow\(^{35}\) are also reported to be involved in genesis of stress induced ulcers. Involvement of free radicals are also reported for gastric ulcers caused by ethanol\(^{35}\) and stress\(^{36}\). Hence diverse mechanisms may be involved in antulcerogenic activity of CPJ.

As genesis of gastric ulcer is thought to be due to an imbalance in offensive and defensive factors, a study on the above parameters in the gastric secretion revealed that CPJ did not show antacid or antiproteic activity, but a significant change in the quality and quantity in dissolved mucin content and decrease in cell shedding was observed. SF showed significant antiproteic activity as seen from the reduction in peptic concentration and output as reported earlier\(^{11}\). The gastric secretion study showed that the concentration of total hexoses, hexosamine and sialic acid were significantly increased signifying the increase in rate of mucin secretion and is further evidenced by an increase in total carbohydrates: protein ratio (TC:P) which is taken as a reliable marker for mucin secretion thus, indicating the enhancement of mucosal resistance factors by CPJ\(^{13}\). The protective effect could also be due to the strengthening of the mucosal barrier as observed from the decrease in DNA content, indicating decreased cell shedding\(^{27}\) and decreased protein content in the gastric juice suggesting decreased leakage from the damaged mucosa by ulcerogens\(^{37}\). The effect of CPJ was comparable to the ulcer protective drug SF.

On the gastric mucosa CPJ significantly increased glycoprotein content as indicated by an increase in the TC:P ratio\(^{27}\). The changes induced by CPJ in the mucosal carbohydrates further corroborate the evidence of increase in mucin secretion and the protection afforded by CPJ to damage by different ulcerogens may be due to its fortification of defensive mucin secretion.

The present study, for the first time reports the antulcerogenic effect of CPJ. The effect may be due to the augmentation of defensive mucosal factors rather than on the offensive factors.

**Acknowledgement**

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**References**