Ethnopharmacological evaluation of antiulcer activity of *Caralluma attenuata*

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**Abstract**

Peptic ulcer is an excoriated area of the gastric or duodenal mucosa caused by action of the gastric juice. It is a chronic, recurrent and the most predominant disease of the gastrointestinal (GI) diseases, which is generally caused by a lack of equilibrium between the gastric aggressive factors and the mucosal defensive factors. Many indigenous Indian medicinal plants have been found to successfully manage GI diseases. In the present study *Caralluma attenuata* (*C. attenuata*) - locally known as ‘Kundaetikommu’ - was studied in the treatment of antiulcer activity with the help of different ulcer models in rats. Rat was sacrificed and stomach was removed for observation of ulcer scores, ulcer index, free acidity, total acidity and pH. The *C. attenuata* maintains the integrity of gastric mucosa by virtue of its effect on offensive and defensive gastric mucosal factors. *C. attenuata* significantly (P<0.05) decreased free acidity, total acidity, ulcer index and gastric volume and significantly (P<0.05) increased the pH whereas ulcer index significantly (P<0.05) decreased in all the ulcer models in rats. Current study shows that *C. attenuata* has the potential to be used as an antiulcer.

**Key-Words:** Gastric ulcer, Peptic ulcer, Antiulcer, Ulcer index, *Caralluma attenuata*

**Introduction**

Gastric ulcer is among the most serious diseases in the world. The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence. A large number of spices and herbs have been evaluated by various researchers for their antiulcer effects to achieve a favorable outcome. Traditional medicinal practitioners have claimed for centuries that extracts from plant (*Caralluma attenuata* [*C. attenuata*]) can be effectively used for the evaluation of different type of ulcers. Despite being one of the well-known medicinal plants used in Indian traditional medicine to treat several ailments, studies pertaining to the pharmacological properties of some medicinal plants are very scarce. *C. attenuata* (Family: Asclepiadaceae) is a thick, succulent perennial herb growing wild in dry hill slope regions of Hyderabad and in several districts of Andhra Pradesh, India. Locally it is known as ‘Kundaetikommu’, and is eaten raw as a cure for diabetes (personal information from users) and the juice of the plant along with black pepper is recommended in the treatment of migraine (Srinivasacharyulu, 1931).

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This plant was found to be a rich source of glycosides (Ramesh et al., 1998). *C. attenuata* was known for the anti-hyperglycemic activity (Venkatesh et al., 2003). The hypoglycemic effect of whole plant *C. attenuata* was investigated in both normal and alloxan induced diabetic rats (Jayakar et al., 2004). Recently Pradeep et al. (2013) reported antidiabetogenic and antioxidant effects of *C. attenuata* extract (CAEt) on streptozotocin-induced diabetes in rats. The present study was undertaken to investigate the ethnopharmacological evaluation of CAEt with a view to provide scientific evidence on modern lines..

**Material and Methods**

**Test animals**

Albino rats (150-175g) were purchased from the animal house of National Laboratory Animal Centre, Lucknow, India. They were maintained in standard environmental conditions and had free access to feed and tap water *ad libitum* during quarantine period. The animals were kept fasting overnight but allowed free access to the water. All studies were performed in accordance with the guidance for care and use of laboratory animals, as adopted and promulgated by the
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Institutional Animal Care Committee, CPCSEA, India (Reg. No. IAEC/NBRI/PH/6-6).

Plant materials and preparation of extract
Fresh whole plants of *C. attenuata* were collected from Ghatkesar, Andhra Pradesh, India. The plant material was identified taxonomically and authenticated by taxonomist in National Botanical Research Institute, Lucknow. The shade dried plant materials were crushed, powdered and exhaustively extracted with 10 volumes of 50% ethanol. The extract was filtered, pooled and concentrated on rotavapour (Buchi, USA) and dried in lyophilizer (Laboconco, USA) under reduced pressure.

Experimental procedure
CAEt in doses of 100 & 250 mg/kg and Omeprazole, the reference drug, in the dose of 20 mg/kg were administered orally twice daily for 5 days for ulcer protective studies. Control group of animals received suspension of 1% CMC in distilled water.

Induction of Ulcer

Pylorus-ligation (PL)-induced ulcers
Gastric ulcers were produced in rats by following method as described earlier by Sanyal et al. (1971). Drugs were administered for a period of 5 days as described above. On day 6 after the last dose, the rats were kept for 18 h fasting and care was taken to avoid coprophagy. Animals were anesthetized using pentobarbitone (35 mg/kg, i.p.), the abdomen was opened and pylorus 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 period. After 4 h, stomachs were dissected out and contents were collected into tubes for estimation of biochemical parameters. The ulcer index was calculated by adding the total number of ulcers per stomach and the total severity of ulcers per stomach. The total severity of the ulcers was determined by recording the severity of each ulcer 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, muscular is remaining unaffected; ++++, ulcer either more than 2 mm in size or perforated with complete destruction of the mucosa with necrosis and hemorrhage, muscular is still remaining unaffected. The pooled group ulcer score was then calculated according to the method of Sanyal et al. (1982). The amount of gastric acid (mL) and the pH values were determined. The total acid secretion in the gastric then was determined in the supernatant volume by titration to pH 7.0 using a 0.01 M NaOH solution, and phenolphthalein as indicator. The assay was performed using the method of Shay et al (1945) with a few modifications.

Aspirin (ASP)-induced ulcers
Aspirin (ASP) was administered orally on the day of experiment in the form of an aqueous water suspension (200 mg/kg, p.o.) and animals were sacrificed after 4 h of administration (Goel et al 1985). The stomach was incised along with the greater curvature and examined for ulcers scores as described under PL-induced ulcers.

Ethanol (EtOH)-induced ulcers
The gastric ulcers were induced in rats by administering (EtOH 1 ml/200 g, i.p.) and the animals were sacrificed by cervical dislocation 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). (Hollander et al 1985)

Cold-restraint stress (CRS)-induced ulcers
On day 6 to 18 h fasted rats, cold restraint stress was given by strapping the rats on a wooden plank and keeping them for 2 h at 4-6 °C. The animals were then sacrificed by cervical dislocation and ulcers were scored on the dissected stomachs as described above.(Gupta et al 1985)

Gastric secretion study
To investigate the anti-secretory activity of CAEt, after removing rats from water, they were anesthetized by diethyl ether; stomach was ligated at lower esophageal sphincter and 2 mL of saline (pH=7.0) infused in the stomach through the pylorus and then gastric content was drained for acid titration. Gastric washout (1 mL) was titrated against 0.01 N of NaOH to endpoint 7.0.

Statistical analysis
The results were expressed as mean ± SEM (n= number of animals in each group) and statistical significance was assessed using one-way analysis of variance (ANOVA) followed by individual comparison by Least Significant Difference test for the determination of level of significance. P values of less than 0.05 were considered to indicate a significant difference between means.

Results and Discussion
CAEt in doses of 100 & 250 mg/kg showed significant gastric ulcer protective effect when given twice daily for 5 days against gastric ulcers induced by ethanol (EtOH), aspirin (ASA), cold restraint stress (CRS) and...
C. attenuata may show the antiulcer activity against both models by generating the prostaglandin which causes inhibition of secretion of gastric fluid. Pretreatment with C. attenuata (100 mg/kg) produced significant decrease in the intensity of gastric mucosal damages induced by the necrotizing agent ethanol compared with control group. A copious amount of gastric mucus is secreted during superficial mucosal damage and provides a favorable microenvironment in repair by restitution. Therefore, it is likelihood that the observed gastric ulcer protection of CAEt provides a general evidence for the close relationship between these factors.

Pyloric ligation-induced ulcers are due to autodigestion of the gastric mucosa and break down of the gastric mucosal barrier (Sairam et al., 2002). Synthetic NSAIDs like aspirin cause mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H+ ions (Rao et al., 2000). The incidence of ethanol-induced ulcers is predominant in the glandular part of stomach was reported to stimulate the formation of leukotriene C4, mast cell secretory products (Oates and Hakkinen, 1988) and reactive oxygen species (Mizui et al., 1987) resulting in the damage of rat gastric mucosa (Peskar et al., 1986). Moreover the result indicates that; in case of pyloric ligation method, the ulcer index, free acidity, total acidity, and volume of gastric juice was significantly(P<0.05) reduced in rats pretreated with CAEt whereas pH was found to be significantly(P<0.05) increased in rats when compared with control group.

Ulcers due to stress are both due to physiological and psychological factors (Miller 1987) and stress plays an important role in etiopathology of gastro-duodenal ulceration. Increase in gastric motility, vagal over activity, (Cho & Ogle, 1979) decreased prostaglandin synthesis (Rao et al., 1999) and mast cell degranulation decreased gastric mucosal blood flow (Hase & Moss, 1973) are involved in genesis of stress induced ulcers. CAEt significantly protect the ulcer induced by cold resistant stress.

Cytoprotective action by drugs has been considered to be due to the generation of prostaglandins or blockade of back diffusion of H+ ions (De et al., 1997) that may be the major mechanism which is responsible for antiulcer activity. The C. attenuata significantly reduced the gastric acid secretion in the present study. The cytoprotective action promotes the generation of prostaglandin, causes decrease in secretion of gastric acid, and significantly reduced the gastric ulceration in pyloric ligated rats without affecting the gastric...
secretion or pepsin. But in case of ethanol-induced method, the cytoprotective action has been decreased by ethanol due to inhibition of synthesis of endogenous prostaglandin which promotes the formation of ulcer. The protective effect of C. attenuata against ethanol induced ulcer in rats may show the anti-ulcer activity by decreasing the ulcer scores. The results further point out that, the cytoprotection may be possible mechanism responsible for the antiulcer activity of the C. attenuata.

Conclusion
In the present study, the C. attenuata shows a potent antiulcer activity, which justifies the ethnopharmacological & traditional medicinal claims. Further investigation is required for the clear understanding of the mechanism of action of C. attenuata with chemically identified active principles.

References

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Table 1: Effect of ethanolic extract of Caralluma attenuata (CAEt)) on ethanol (EtOH), aspirin (ASA), cold restraint stress (CRS) and pylorus ligation (PL) induced gastric ulcers in rats

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>EtoH</th>
<th>ASA</th>
<th>CRS</th>
<th>PL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>27.05±2.48</td>
<td>13.57±1.48</td>
<td>22.33±1.83</td>
<td>16.3±1.95</td>
</tr>
<tr>
<td>CAEt 100mg</td>
<td>11.57±1.90*</td>
<td>6.28±0.9*</td>
<td>11.45±1.29*</td>
<td>5.5±1.21*</td>
</tr>
<tr>
<td>CAEt 250mg</td>
<td>8.68±1.50*</td>
<td>5.15±0.59*</td>
<td>10.03±1.45*</td>
<td>4.55±1.04*</td>
</tr>
<tr>
<td>Omeprazole 20mg</td>
<td>6.45±1.32*</td>
<td>2.32±0.47*</td>
<td>6.8±1.16*</td>
<td>3.18±0.86*</td>
</tr>
</tbody>
</table>

*P<0.05, as compared to their respective control. Data are mean±S.E.M. n=6 in each group

Table 2 : Effect of ethanolic extract of Caralluma attenuata (CAEt)) on pH, free acidity and total acidity in in pylorus ligation induced ulcer model

<table>
<thead>
<tr>
<th>Treatment (mg/kg)</th>
<th>Volume (ml/100g)</th>
<th>pH</th>
<th>Free Acidity ((mEq/l/100g)</th>
<th>Total Acidity ((mEq/l/100g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>2.95±0.26</td>
<td>1.48±0.08</td>
<td>74.98±1.87</td>
<td>94.03±5.3</td>
</tr>
<tr>
<td>CAE 250mg</td>
<td>0.77±0.14*</td>
<td>3.93±0.18*</td>
<td>22.9±1.5*</td>
<td>31.94±1.74*</td>
</tr>
<tr>
<td>Omeprazole 20mg</td>
<td>0.43±0.04*</td>
<td>4.28±0.22*</td>
<td>16.4±1.43*</td>
<td>25.38±1.98*</td>
</tr>
</tbody>
</table>

*P<0.05, as compared to their respective control. Data are mean±S.E.M. n=6 in each group

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