Research Article [Garg *et al.*, 5(6): June, 2014:3585-3589]
CODEN (USA): IJPLCP ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES
(Int. J. of Pharm. Life Sci.)

Ethnopharmacological evaluation of antiulcer activity of *Caralluma attenuta*

Sunil Garg[1*], Kishan Pal[2], Alok Sharma[3] and Kavita Garg[4]
1, Department of Pharmacy, Mewar University - India
2, Department of Biotechnology, Sri Ram College of Pharmacy, (UP) - India
3, DIL India Ltd. - India
4, INC Research, Gurgoan - India

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).

*** Corresponding Author**
E-mail: sunilgarg_in@yahoo.com

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

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 & 250mg/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 anaesthetized 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 0.01M 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, 1) 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 & 250mg/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

pyloric ligation (PL). (Table 1) Omeprazole also show similar effects but was more effective compared with *C. attenuata*.

Effect on anti-secretory parameters

Estimation of gastric juice of CAEt treated groups indicated that there was a significant decrease in the free acidity and total acidity of the gastric juice.

Rats treated with 100 mg/kg and 250 mg/kg of CAEt showed a significant decrease in gastric volume, free acidity and total acidity ($p<0.05$) and was comparable to that of the Omeprazole treated group ($p<0.05$) of rats (Table 2). The pH was significantly increased when compared with control group. Omeprazole showed similar effects but was more effective as compared to *C. attenuata*.

There are several factors that may induce ulcer in human being such as stress, chronic use of anti-inflammatory drugs and continuous alcohol ingestion, among others (Barocelli et al., 1997). Although in most cases the etiology of ulcer is unknown, it is generally accepted that it is the result of an imbalance between aggressive factors and maintenance of the mucosal integrity through the endogenous defense mechanism (Piper & Stiel, 1986 and Sergio et al., 2007). The etiology of gastro-duodenal ulcers is influenced by various aggressive and defensive factors such as acid–pepsin secretion, parietal cell, mucosal barrier, mucus secretion, blood flow, cellular regeneration and endogenous protective agents such as prostaglandins and epidermic growth factors (Repetto & Llesuy, 2002). Some other factors, such as inadequate dietary habits, excessive ingestion of non-steroidal anti-inflammatory agents, stress, hereditary predisposition and infection by *Helicobacter pylori*, may be responsible for the development of peptic ulcer (Peckenpaugh & Poleman, 1997).

The present study showed that the ethanolic extract of *C.attenuata* possess gastroprotective activity as evidenced by its significant inhibition in the formation of ulcers induced by various physical and chemical agents. The incidence of ethanol-induced ulcers is predominant in the glandular part of stomach was reported to stimulate the formation of leukotriene C4. Ethanol-induced depletion of gastric wall mucus has been prevented by CAEt. It implies that a concomitant increase in prostaglandins (Pihan et al., 1986) or sulfhydryl compounds (Szabo et al., 1981) contribute to protect the stomach from ethanol injury. In ethanol-induced ulcer, the ulcer scores were significantly ($P<0.05$) decreased in rats pretreated with *C. attenuata* which were compared with control group.

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.

Pylorus 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 where as 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

1. Barocelli E, Chiavarini M, Ballabeni V, Barlocco D. Vianello P, Dal Piaz V, Impicciatore M. Study of the antisecretory and antiulcer mechanism of new indenopyridazinone derivative in rats. Pharmacol Res (1997) 35: 487 - 492.
2. De B, Maiti RN, Joshi VK, Agrawal VK, Goel RK. Effect of some Sitavirya drugs on gastric secretion and ulceration. Ind J Expt Biol (1997) 35:1084 - 1087.
3. Cho CH, Ogle CW. Cholinergic-mediated gastric mast cell degranulation with subsequent histamine H1 and H2-receptor activation in stress ulceration in rats. European Journal of Pharmacology. 1979; 55:23-33.
4. Gupta MB, Nath R, Gupta GP, Bhargava KP. A study of the antiulcer activity of diazepam and other tranquillosedatives in albino rats. Clinical and Experimental Pharmacology. 1985; 12: 61- 63.
5. Hase T, Moss BJ. Microvascular changes of gastric mucosa in development of stress ulcers in rats. Gastroenterology. 1973; 65:224-322.
6. Hollander D, Taranawski A, Krause WJ & Gergely H. Protective effect of sucralfate against alcohol-induced gastric mucosal injury in the rat. Gastroenterology (1985); 88: 366-374.
7. Jayakar B, Rajkapoor B, Suresh B. Effect of *Caralluma attenuata* in normal and alloxan induced diabetic rats. J Herb Pharmacother (2004) 4: 35-40.
8. Kumar P, Sharma A, Varshney P, Rao CV. Antidiabetogenic and antioxidant effects of *Caralluma attenuata* extract on streptozotocin induced diabetes in rats. J Pharmacy Res (2013) vol. 6/7 (3):257-262.
9. Miller TA. Mechanisms of stress-related mucosal damage. American Journal of Medicine. 1987; 83:8-14.
10. Mizui T, Sato H, Hirose F, Doteuchi M. Effect of antiperoxidative drugs on gastric damage induced by ethanol in rats. Life Sci (1987) 41 : 755–763.
11. Oates PJ, Hakkinen JP. Studies on the mechanism of ethanol induced gastric damage in rats. Gastroenterology (1988) 94: 10–21.
12. Peckenpaugh NJ, Poleman CM. Nutricao: Essencia Dietoterapia (1997) 7th ed. Roca, Sao Paulo.
13. Peskar BM, Lange K, Hoppe U, Peskar BA. Ethanol stimulates formation of leukotriene C_4 in rat gastric mucosa. Prostaglandins (1986) 31: 283-293.
14. Pihan G, Majzoubi D, Haudenschild C, Trier JS, Szabo S .Early microciculatory stasis in acute gastric mucosal injury in the rat and prevention by 16,6 dimethyl prostaglandin E2 or sodium thiosulfate. Gastroenterology (1986) 91: 1415–1426.
15. Piper DW, Stiel DD. Pathogenesis of chronic peptic ulcer, current thinking and clinical implications. Medical Progress (1986) 2: 7-10.
16. Ramesh M, Rao YN, Rao AV, Prabhakar MC, Rao CS, Muralidhar N, Reddy BM. Antinociceptive and anti-inflammatory activity of flavonoids isolated from *Caralluma attenuata* J Ethnopharmacol (1998) 62: 63-66.
17. Rao CV, Sairam K, Goel RK,. Experimental evaluation of *Bacopa monnieraon* rat gastric ulceration and secretion. Ind J of Physio and Pharmacol (2000) 44: 35–41.
18. Rao ChV, Maiti RN, Goel RK. Effect of mild irritant on gastric mucosal offensive and defensive factors. Indian Journal of Physiology and Pharmacology. 1999; 44; 185-191.
19. Repetto MG, Llesuy SF. Antioxidant properties of natural compounds used in popular medicine for gastric ulcers. Braz J Med Biol Res (2002) 35: 523–534.
20. Sairam K, Rao ChV, Dora Babu M, Agrawal VK, Goel RK. Antiulcerogenic activity of methanolic extract of *Emblica officinalis*. J of Ethnopharmacol (2002) 82/1: 1–9.

21. Sergio FA, Marivane L, Eros C, Vania FN, Valdir CF, Rivaldo N. Evaluation of the antiulcerogenic activity of Maytenus robusta (Celastraceae) in different experimental ulcer models. J Ethnopharmacol (2007) 113: 252–257.
22. Shay H, Komarov SA, Fels SS, Meranze D, Gruenstein M, Siplet H. A Simple Method for the Uniform Production of Gastric Ulceration in the Rat Gastroenterol (1945) 5:43.
23. Srinivasacharyulu, Y. Yogarathnakaram Swatantra Press, Nellore, India pp (1931) v2: 678.
24. Sanyal AK, Pandey BL, Goel RK. The effect of a traditional preparation of copper, tamrabhasma, on experimental ulcers and gastric secretion. Journal of ethnopharmacology. 1982; 5:79- 89.
25. Szabo S, Trier JS, Frankel PW. Cysteamine induced acute and chronic duodenal ulcer in the rat. American J of Patho (1981) 93: 273-276.
26. Venkatesh S, Reddy GD, Reddy BM, Ramesh M, Rao AV Antihyper-glycemic activity of *Caralluma attenuata*. Fitoterapia (2003) 74: 274-279.

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

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

***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

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

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

How to cite this article
Garg S., Pal K., Sharma A. and Garg K. (2014). Ethnopharmacological evaluation of antiulcer activity of *Caralluma attenuata*. *Int. J. Pharm. Life Sci.*, 5(6):3585-3589.
Source of Support: Nil; Conflict of Interest: None declared

Received: 25.05.14; Revised: 30.05.14; Accepted:07.06.14