ANTISECRETORY AND ANTIULCER ACTIVITY OF ACACIA CATECHU AGAINST INDOMETHACIN PLUS PYLORIC LIGATION INDUCED GASTRIC ULCERS IN RATS

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Abstract: Study was aimed to evaluate the possible antisecretory and antiulcer activity of crude bark extract of Acacia catechu and its action against indomethacin an non steroidal anti inflammatory drug (NSAID) plus pyloric - ligation induced gastric ulcers in rats. Administration of crude extract of Acacia catechu (400mg/kg/day p.o.) significantly reduced ulcer index when compared with indomethacin induced gastric ulcerative rats. Ranitidine (30 mg/kg/day p.o.) was used as the reference antiulcer drug. Extract treated animals also significantly reduced volume of gastric secretion, free acidity and total acidity. A significant increase in total carbohydrate (TC) / total protein (TP) ratio of gastric juice was also observed. No significant change in the total protein was noted during the study. Acacia catechu was found to be an effective antiulcerogenic agent. The result of this study suggests that Acacia catechu cause an inhibitory effect on release gastric hydrochloric acids and protects gastric mucosal damage.

Key words: Acacia Catechu, Indomethacin plus Pyloric – Ligation, Ranitidine, Antiulcer

INTRODUCTION

Peptic ulcer is a gastrointestinal disorder that requires a well targeted therapeutic strategy. A number of drugs including proton pump inhibitors and H₂ receptor antagonists are available for the treatment of peptic ulcer, but clinical evaluation of these drugs has shown incidence of relapses, side effects and drug interactions [1]. That is the rationale for the development of new anti-ulcer drugs, and the search for novel molecules has been extended to herbal drugs that would offer better protection and decreased relapse. Drugs of plant origin are increasing in popularity and are being investigated for a number of disorders, including peptic ulcer [2]. The dried bark of Acacia catechu (family: leguminosae, sub family: mimosiasae) commonly known as Katha or Karangali is widely used in India for its various pharmacological effects [3]. This plant material is used as anodyne, astringent, bactericide, refrigerant, stimulant, styptic, masticatory expectorant and antiphlogistic [4]. It is also used in asthma, cough, bronchitis, colic, diarrhoea, dysentery, boils, in skin affections and sores and for somatitis [5]. The bark is used as an anthelmentic, antipyretic, antiinflammatory, in bronchitis, ulcers, anaemia and gum troubles [3]. The important chemical constituents reported in the heartwood are catechin, catechutannic acid, epicatechin, catechin tetramer, dicatechin, gallicatechin, kaempferol, taxifolin, isorhamnetin, (+) afzelechinn, L - arabinose, D - galactose, D - rhamnose and aldobiuronic acid [3]. The medicinal properties of Acacia catechu may be due to the antioxidant properties of these constituents [6].

MATERIALS AND METHODS

Chemicals: Chemicals were procured locally Indomethacin (Bombay tablet Mfg. co., Gandhinagar); Carboxy Methyl Cellulose (CMC; Apex Chemicals, Mumbai) and Diethyl Ether (Alembic Chemicals work Ltd., Baroda).
Animals: Adult (one and half month old, body weight 225 to 275 g) albino rats (Wistar strain) of the either sex were used in the present study. The animals were acclimatized for ten days in polyutharine cages in laboratory conditions. All the rats were fed with standard laboratory diet and given water ad libitum. Care was taken to avoid coprophagy.

Drug preparation: Hydroalcoholic extract of bark of Acacia catechu (prepared by continuous soxholet method) (400 mg/ml) were suspended in 0.5% CMC in distilled water.

Indomethacin plus pyloric ligation (PL) induced gastric ulceration model: Rats were fasted for 12 hours, and treated with two oral doses (2 X 10 mg/kg) of indomethacin suspension (in 0.5% CMC made in water) as a standard dose, at an interval of fifteen hours, two hours after the second dose of indomethacin, PL was carried out [7] as per the method of Shay et al. [8]. Four hours after ligation, the rats were destroyed by over-dose of anesthetic ether. Pyloric ligation was done only to collect the gastric content for analysis. The stomach was dissected out by its greater curvature and contents were drained into sterile tubing. The inner surface of the empty stomach was examined for gastric lesions.

Experimental protocol: Rats were divided into 4 groups (n 6). Rats of group I were given only vehicle (0.5% CMC in water p. o.) each day for up to fifteen days followed by normal laboratory diet; group II were given standard doses of indomethacin (2 X 10 mg/kg p.o.) followed by normal laboratory diet for fifteen days; group III animals were given standard doses of indomethacin (2 X 10 mg/kg p.o.) plus drug (Acacia catechu extract- 400 mg/Kg/day p.o.) for fifteen days followed by normal laboratory diet; group IV was given standard doses of indomethacin (2 X 10 mg/kg p.o.) plus ranitidine (30 mg/kg/day orally) for fifteen days followed by normal laboratory diet.

On day 16th PL was performed and rats were sacrificed and stomachs were removed. Ulcer index [9], volume of gastric secretion [10], free acidity and total acidity [11], total carbohydrate (TC) content [12] and total protein (TP) content [13] and TC/TP ratio of gastric juice were estimated.

Statistical Analysis: The results were expressed as mean ± SEM. The significance of difference between mean values for the various treatments was tested using unpaired t test. The level of significance was P < 0.05 [14].

RESULTS

The results of drug treated animals were compared with indomethacin treated animals. Figure 1a-b shows the effect of extract on ulcer index and volume of gastric secretion in the experimental animals. In group II animals, treated with indomethacin volume of gastric secretion (2.860 ± 0.236) is significantly higher when compared with control (group I only vehicle treated animals). In group III and group IV of animals treated with Acacia catechu and ranitidine respectively the volume of gastric secretion (2.380 ± 0.060, 1.960 ± 0.230) was significantly reduced. In group II animals ulcer index was significantly higher (5.977 ± 0.520) when it was compared with group I but in group III and group IV the ulcer index was significantly reduced (3.390 ± 0.660; 1.960 ± 0.230 respectively) (Fig. 1b).

The crude extract of Acacia catechu significantly decreases free acidity (10.98 ± 1.097) and total acidity (37.82 ± 3.020) (Fig.2a,b) and significantly increases total carbohydrate (TC) content (424.000 ± 8.510) (Figs.3ab) and TC/TP ratio (1.087 ± 0.080) (Figs. 4) of gastric juice. No significant effect on the TP has been observed (Fig. 3b).

DISCUSSION

Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used in the treatment of pain, fever and inflammation [15]. However, these drugs have some side effects, especially on the gastrointestinal tract. NSAIDs like indomethacin inhibits COX - 1 thereby inhibits the prostaglandin synthesis, consequently lipoxygenase pathway is enhanced liberating leukotrienes and these leukotrienes are reported to have a role in ulcerogenesis. In addition there is some evidence that NSAIDs may induce ulcer by causing the back diffusion of H+ ion in to mucosal cells. Therefore, the gastroprotective effect of the test extract may be due to its ability to inhibit the synthesis of prostaglandins/leukotrienes [16].

Results of the study suggest that the extract can be used for the prevention and treatment of gastric ulcers. In this study, fifteen days treatment with administration of NSAIDs such as indomethacin followed by pyloric ligation produced severe gastric
Figs. 1a and 1b: Effect of *Acacia catechu* extract on ulcer Index (a) and gastric secretion (b). All values are represented as mean ± SEM (n = 6). P Values: +++ < 0.001 When compared with control untreated animals. *** < 0.001 When compared with indomethacin induced animals.

Figs. 2a and 2b: Effect of *Acacia catechu* extract on Free acid (a) and total acid (b). All values are represented as mean ± SEM (n = 6). P Values: +++ < 0.001 When compared with control untreated animals. *** < 0.001 When compared with indomethacin induced animals.
lesions in the rat’s stomach. Indomethacin has been shown to inhibit gastric bicarbonate secretion in vitro [17]. Increased gastric acid secretion is strongly implicated in development of gastric ulcers by anti-inflammatory drugs [18]. Present investigation also confirmed the crucial role of hydrochloric acid in ulceration. Indomethacin and PL induced lesions were associated with significant increase in volume of gastric secretion, free and total acidity of gastric juice, and decrease in TC and TC/TP ratio.

Administration of crude extract of Acacia catechu daily for fifteen days showed significant decrease in gastric volume secretion, ulcer index, free acidity and total acidity of gastric juice in all experimental animal models, suggesting antisecretory and antiulcer effect of the drug. Treatment with crude extract of Acacia catechu daily for fifteen days showed significant increase in TC and TC/TP ratio of gastric juice. Increase in TC/TP ratio is important for evaluating antiulcer activity [19,20] by effect on the mucus formation in the stomach.

The present study thus confirms antiulcer and antisecretory effects of Acacia catechu in indomethacin-induced gastric lesions. In our opinion, Acacia catechu causes inhibitory effects on the release of gastric hydrochloric acid, to protect against gastric mucosal damage. However, more studies are necessary to show the reproducibility of our results.
REFERENCES