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Antiulcerogenic Activity of *Caesalpinia Pulcherrima* Leaves

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Abstract

Peptic ulcer disease (PUD) is one of the leading diseases throughout the world that requires a rational therapy for better therapeutic effect. Use of conventional drug regimen used as an antiulcer like; proton pump inhibitor, H_2 antagonist shown incidence of relapses, side effect, and drug interaction. The use of herbal drug is the choice of drug for all kind of diseases, especially in peptic ulcer disease. This study was undertaken to evaluate the potential of anti-ulcerogenic activity of leaves of *Caesalpinia pulcherrima* in ethanolic extract. The ethanolic extract of *Caesalpinia pulcherrima* was found to be significant at 500 mg/kg b.wt. in aspirin induced ulcer model in rat. The parameter evaluated as ulcer index, gastric volume, pH, content of tissue glutathione, acidic volume, total protein was recorded. In aspirin induced model, a decrease in ulcer index, total acidity, total volume of gastric secretion and increase in total protein, glutathione content and pH of gastric secretion when compared with toxic was observed. It is concluded that the ethanolic extract of *Caesalpinia pulcherrima* was found to be significant at dose of 500mg/kg as an anti-ulcerogenic.

Keywords: *Caesalpinia pulcherrima, glutathione (GSH), ulcer index, Asprin*

Introduction

The pathophysiology of peptic ulcer disease is an imbalance between mucosal defense factors (prostaglandin, nitric oxide, bicarbonate, mucin, and other peptides and growth factors) and injurious factors (acid and pepsin). Mostly duodenal ulcers patients produce more acid than do control individual, particularly at night (basal secretion). [1] Although gastric ulcers patients either normal or diminished acid production. The ulcer may be caused due to a weakened mucosal defense and reduced bicarbonate production contributes. Up to 60% of peptic ulcers are associated with *H. pylori* infection of the stomach which causes destruction of somatostatin cells. [2] This resulting into a defect in the regulation of gastrin production by stomach, Gastrin stimulates the production of gastric acid by parietal cells and, in *Helicobacter pylori* colonization responses increases gastrin. The increases in acid can contribute to the erosion of the mucosa and therefore ulcer formation. In patient receiving chronic NSAIDs therapy, ulcers occur more frequently in the stomach than in the duodenum. [3] Major biochemical changes induced by aspirin and other NSAIDs are denaturation of mucus glycoprotein in that area of the mucosa. Further discharge of mucus from epithelial cells leads to mucosal damage including bleeding and erosion. *Caesalpinia pulcherrima* is a 3m tall shrub; the flowers are borne in racemes up to 20 cm long, each flower with five yellow, orange or red petals. The flowers are bowl shaped, 2-3" across, with five crinkled, unequal red and orange petals, and ten prominent bright red stamens that extend way beyond the corolla. [4] Plants belonging to the family Caesalpiniaceae have wide range of medicinal uses. Caesalpinia pulcherrima vernacularly known as Peacock Flower is widely distributed in India and its leaves, flower, bark and seeds are used in Indian medicine. [5] The bark is used as abortifacient while leaves are used as cathartic. [6] The flowers used for intestinal worms, cough, catarrh. The leaf and flower extract are used as antibacterial against gram positive bacteria. The juice from the leaves is said to cure fever, the juice from the flower is said to cure sores, and the seeds are said to cure bad cough, breathing difficulty, and chest pain. Four grams from the root is also said to induce abortion in the first trimester of pregnancy. [7] Previously, no scientific work has been reported on the anti-ulcer activity of leaves of *Caesalpinia pulcherrima* plant. The present study was therefore undertaken to evaluate the anti-ulcer

activity of *Caesalpinia pulcherrima* extract on albino rat. In this study, various study parameters like ulcer index, gastric volume, pH, total acidity, glutathione, and total protein estimation was studied.

Materials and Methods

Animals

Albino Wistar rats weighing 200–250 g rats weighing of either sex were obtained from Wockhardt Ltd. Aurangabad. The animal had free access to standard pellet diet and water *ad libitum*. All procedures were performed in accordance with the Institutional Animal Ethics Committee (IAEC) constituted as per the direction of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Authentification & Collection Of Plant

The fresh plant of *Caesalpinia Pulcherrima* belonging to the family *Fabaceae* was collected from the local area of Aurangabad, Maharashtra. The plant was identified and authenticated by Dr. A.S. Dhabe, Department of Botany, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad.

Extraction and Preparation of Test Sample

The dried powdered leaves of *Caesalpinia Pulcherrima* plant was weighed (360 g). A 95% w/v ethanolic extract was prepared by soxhlet extraction method. The dried powdered leaves of *Caesalpinia Pulcherrima* were extracted with 95% v/v ethanol for 36 hr using soxhlet extractor. The combined extracts were concentrated at 40°C to obtain dark brownish residue. The yield obtained from the above process was found to be 1.8% w/w. The extracts were preserved in a refrigerator for further use.

Dose Fixation

Toxicity study - up and down procedure was carried out as per the guidelines set by Organization for Economic Co-operation and Development (OECD). Chronic oral toxicity study was done according to OECD guidelines 423. In this experiment two groups of Wistar rats (n=3) were used. Animals were fasted overnight with water *ad libitum* and food was withheld for 3-4 hrs after oral administration of the extracts. One group of animals were treated with starting dose of 2000 mg/kg b.w. orally and the maximum dose of 5000 mg/kg b.w. was administered to rats, another group was treated with normal saline. Observation includes mortality and clinical signs, which includes changes in skin fur, eyes and mucous membranes. The gross behaviors like body positions, locomotion, rearing, tremors, gait was observed.

Route of Administration

The ulcer inducing agents, standard drugs & extracts of *Caesalpinia Pulcherrima* were administered orally.

Statistical Analysis

Statistical analyses were carried out by using with one-way ANOVA followed by Dunnett's test at level of significance $P<0.05$. All data were shown as the mean $\pm$ SEM. Statistical analysis was performed using prism-5 statistical software (USA). [8]

Aspirin Induced Gastric Ulcer

Aspirin suspended in 5% gum arabic solution was given orally at 200 mg/kg to rats. Five hr later, the animals were sacrificed under ether anesthesia and the stomachs were removed. The stomach was inflated by injecting with 10 ml of saline through the esophageal junction and immersed in 5% neutral formalin solution for 10 min to fix the outer layer of the gastric wall. Subsequently, the stomach was incised along the greater curvature and the length of each lesion in the glandular portion was measured under a dissecting microscope (10 x). The sum of the length (mm) of all lesions for each rat was used as an ulcer index. The test drugs were given orally using a gastric tube 30 min before the administration of aspirin. [9]

Grouping of Animals

Group I : Animals served as control and received 0.1% Tween-80 (10 ml/kg p.o.).
Group II: Animals received suspension of Aspirin in gum Arabica (200 mg/kg p.o.).
Group III: Animals received standard drug Famotidine (30 mg/ Kg p.o.) + Aspirin.
Group IV: Animals received ethanol extract of C.Pulcherrima leaves suspended in tween 80 (500mg/ Kg p.o.) + Aspirin.

Results

The present study has been undertaken to evaluate the antiulcer effect of ethanolic extracts of leaves of *Caesalpinia pulcherrima* on aspirin induced ulcer healing effect. The results obtained from the present study have shown that EECP leaves of *Caesalpinia pulcherrima* possess antiulcer effect on aspirin induced ulcer. In aspirin induced model, a decrease in ulcer index, total acidity, total volume of gastric secretion and increase in total protein, glutathione content and pH of gastric secretion when compared with toxic was observed.

Table 1: Effect of Ethanolic extract of C.pulcherrima of leaves on ulcer index, gastric volume, and pH against aspirin induced gastric ulcer in rats.

Group	Treatment	Ulcer index	Gastric volume (ml)	pH
I	Control	2.89 ± 0.14**	3.49 ± 0.16*	3.18 ± 0.07*
II	Toxic (Aspirin 150mg/kg)	16.04 ± 0.16	2.50 ± 0.13	2.43 ± 0.19
III	Standard (famotidine 30 mg/kg)	4.56 ± 0.13**	0.71 ± 0.07**	4.88 ± 0.08**
IV	CPLE 500mg/kg + Aspirin 150mg/kg	6.67 ± 0.14**	1.28 ± 0.09*	3.55 ± 0.15*

Results are expressed as Mean ± SEM, Data was analyzed by one way ANOVA followed by Dunnett's test. Comparisons were made with toxic group vs. all treated groups, * and ** represents statistical significance at P < 0.05 and P < 0.01.
CPLE: C. pulcherrima leaves extract.

Table 2: Effect of EECP of leaves on total acidity, tissue glutathione, and total protein against aspirin induced gastric ulcer in rats

Group	Treatment	Total Acidity	Tissue Glutathione	Total protein
I	Control	63.83 ± 1.51**	42.91 ± 0.47*	5.88 ± 0.19**
II	Toxic (Aspirin 150mg/kg)	37.00 ± 0.68	25.46 ± 0.32	4.32 ± 0.02
III	Standard (famotidine 30mg/kg)	16.66 ± 0.84**	41.17 ± 0.20*	6.85 ± 0.03**
IV	CPLE 500mg/kg + Aspirin 150mg/kg	28.66 ± 0.61*	32.80 ± 0.26**	6.52 ± 0.02*

Results are expressed as Mean ± SEM, Data was analyzed by one way ANOVA followed by Dunnett's test. Comparisons were made with toxic group vs. all treated groups, * and ** represents statistical significance at P < 0.05 and P < 0.01.
CPLE: C.pulcherrima leaves extract.

Histopathology

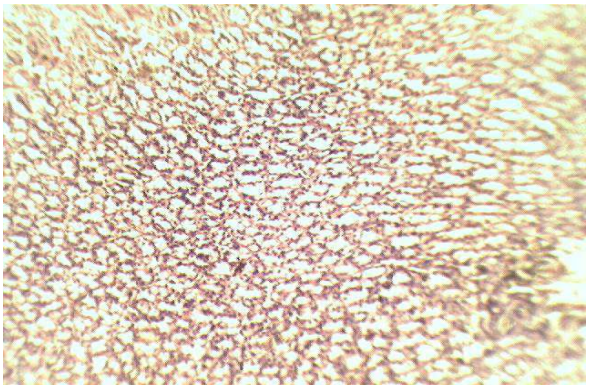

Fig 01. Group I (Normal)– shows normal stomach

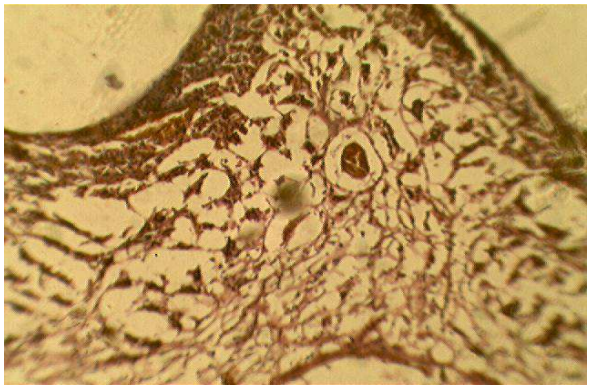

Fig 02. Group II (Aspirin induced ulcer) – shows hemorrhage and discontinuity in the lining epithelium

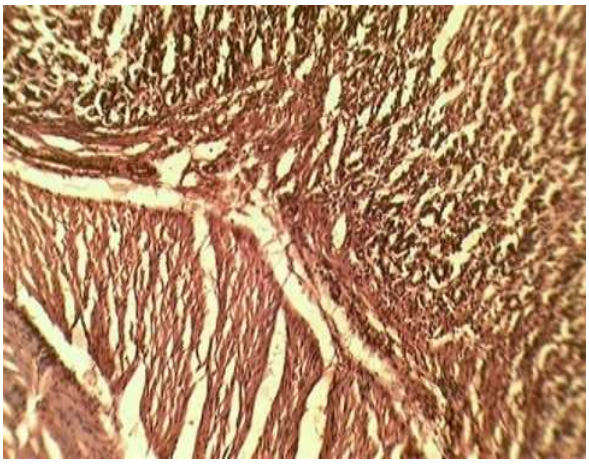

Fig 03. Group III (Aspirin + Famotidin 30mg/kg) – stomach shows normal glandular mucosa with underneath coats.

hyperplasic mucosal glands.

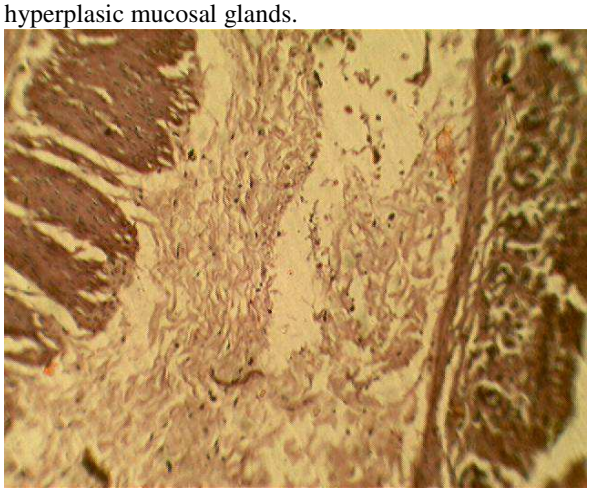

Fig 04. Group IV (Aspirin + EECP leaves 500mg/kg) – stomach shows areas of ulceration of glandular mucosa and congested blood vessels.

Discussion

Peptic ulcer is a chronic and appealing disease. Today, it is dominant among the diseases that affect the world's population. The principal factors causing this disease are inadequate dietetic habits, prolonged use of NSAIDs drugs, stress and infection by *Helicobacter pylori,* in addition to other factors of genetic origin. The important roles of oxygen-derived reactive oxygen species (ROS) and lipid peroxides (LPO) in acute gastric lesions, which are induced by NSAIDs such as aspirin, have been supported by experimental data. Aspirin has been shown to produce higher gastric damage in rats when compared to other NSAIDs, for this reason it has become the preferred drug for inducing ulcer models, in many experimental studies. Antidepressant drugs have been shown to produce antiulcer effects by reducing histamine secretion from mast cells, inhibiting gastric acid secretion, and blocking leukotriene (LTC_4, D_4, and E_4) receptors. The pathogenesis of gastro duodenal ulcers are influenced by various aggressive and defensive factors, such as mucus secretion, mucosal barrier, acid pepsin secretion, blood flow, cellular regeneration and endogenous protective agents (prostaglandins and epidermal growth factor). [10]

Treatment of rats with aspirin, a non-selective cyclooxygenase inhibitor is known to induce gastric damage through multiple mechanisms which include suppression of prostaglandin generation, overproduction of leukotrienes, acting as a topical irritant and by reducing the local blood-flow. EECP and famotidine pretreatment has reduced the lesion-producing effect of aspirin, and significantly prevented depletion of PGE_2-like activity by the latter in the areas of mucosal damage. Rats pretreated with EECP produced significant protection in this model. It is possible that an enhanced level of gastric mucus, generating prostaglandins and inhibiting leukotriene may contribute to the gastro protective effect of EECP. Since EECP markedly inhibited gastric acid secretion and luminal ulcers in aspirin induced gastric ulcer rats, this observed effect could be related, at least in part, to the ability of EECP to reduce gastric acid secretion. It is now accepted that gastric acid secretion plays an important role in the progression from an erosive mucus layer to a gastric lesion. [11] On the other hand, substances which have the ability to suppress gastric acid secretion, such as proton pump inhibitors and histamine H_2-receptor antagonists are believed to accelerate the healing process of the gastric lesions or inhibit the formation of mucosal injury. With the ever growing interest in natural medicine, many plants have been screened and reported to be useful in treating and managing ulcer. *Caesalpinia pulcherrima* have several pharmacological properties including anti-inflammatory, [12] anti-oxidant [13] and anti-microbial. [14] From the above discussion it is evident that EECP treatment caused a significant decrease in total acidity, gastric volume, ulcer score, and increasing rate of pH, glutathione, total protein in both ethanol

and aspirin induced models. These results indicate that EECP treatment lowers the risk and incidence of ulcers as well as helps in treatment of active ulcers. In this study EECP shows increase in glutathione content in gastric mucosa. Reduction in ulcer index shows that EECP treatment cures active ulcers. Increase in total protein correlates the reduction of peptic activity and suggests that EECP has an active role in stopping the proliferation of ulcers. Decrease in gastric volume indicates that EECP is effective in lowering the formation of pepsin, because high acid volume with a low pH is required for the activation of pepsinogen to pepsin. Hence EECP treatment is effective in the prophylaxis as well as treatment of ulcers. [15]

Conclusion

According to the study conducted, it is revealed that the ethanolic extract of *Caesalpinia pulcherrima* was found to be significant at 500 mg/kg b.wt. in aspirin induced model in rat. As it is shown in the study that a decrease in ulcer index, total acidity, total volume of gastric secretion and increase in total protein, glutathione content and pH of gastric secretion when compared with toxic.

"Cite this Article"

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