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ANTIULCER ACTIVITY OF *CINNAMOMUM TAMALA LINN.* LEAVES EXTRACT IN EXPERIMENTAL ANIMAL

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ABSTRACT

The present investigation is an attempt to utilize the herbal flora for gastrointestinal disorder like ulcer and their respective therapeutic effect on human sufferings. Herbal medicines are easily acceptable by the people. These are also available at low cost and are comparatively safe. The additive and synergic action of polyherbal preparation prevents the side effects compared to isolated active compound(s).This study was carried out to evaluate the antiulcer activity of ethanolic extract of the leaves of *Cinnamomum tamala Linn* in experimental animals. The antiulcer activity of *Cinnamomum tamala Linn* were studied against Pylorus ligated, Aspirin, Ethanol induced ulcers in male Sprague – Dawley rats. It was revealed that administration of ethanolic extract of leaves of *Cinnamomum tamala Linn* in preventing and healing ulcers is based on its ability to stimulate mucus synthesis as well as on the stimulation of an antisecretory effect.

Key words: Aspirin, *Cinnamomum tamala Linn*, Ethanol induced ulcers, Pylorus ligated ulcer, Ranitidine, Ulcer index.

INTRODUCTION

Herbal remedies used for primary health care are the best and safest than instant relief giving allopathic drugs. Therefore the present project is proposed the treatment of gastrointestinal disorder like ulcer. Peptic ulcer represents a major health problem, both in terms of morbidity and mortality. Neurotransmitters or harmones that directly stimulate secretion of hydrochloric acid and pepsin by the gastric glands are acetylcholine, gastrin and histamine. Activity of the gastric secretary cells has been found to be stimulated by caffeine, alcohol, hydroalcoholic acid, sodium chloride, non steroidal anti- inflammatory drugs NSAID's) and stress [1-5].

Several components of gastric mucosal defense are influenced or mediated by prostaglandin, including mucus and bicarbonate secretion, blood flow, epithelial cell turnover and repair, and immunocyte function. Endogenous substances such as nitric oxide, polypeptides such as substance P and endothelin, autocoid comprising platelet activating factor, leukotrienes, serotonin, histamine and reactive oxygen species have also been found to play an important role in the gastroduodenal lesion [6, 9].

Increased gastric motility, vagal over activity, mast cell degranulation, decreased gastric mucosal blood flow and decreased prostaglandin level during stress condition are thought to be involved in ulcer generation. Similarly role of oxygen derived free radicals have been shown to play a role in experimental gastric damage induced by ischemia and reperfusion, hemorrhagic shock and ethanol administration. Helicobacter pylori a pathogen is now known to be the most common and important caused of gastric ulcer in humans, exhibits active inflammation with epithelial damage accompanied by neutrophil migration [10].

No acid – No ulcer has dominated the pharmacological basis of ulcer therapy, and the drugs used reduced acid secretion. Not all patients, however, with gastric or duodenal ulcer have high acid secretion. In fact, only 30 % - 40 % of cases with duodenal ulcer have hypersecretion of gastric acid and, in patients with gastric ulcer, acid secretion is either normal or low. In these cases, decreased mucosal resistance might be the dominant factor. Peptic ulceration results from an imbalance between acid – pepsin secretion and mucosal resistance. Since gastric acid is one of the major aggressive factor contributing to peptic ulcer disease, the reduction of gastric acid either by surgical or pharmacological intervention has been used to promote ulcer healing.

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Surgical treatment of peptic ulceration is usually either by vagotomy or removal of the diseased portion of the stomach [11-15].

MATERIALS AND METHODS

Plant material and extraction

The dried plant materials used in this study were leaves of *C.tamala* (Family: *Lauraceae)* collected from the local market of Lucknow, India. The plant material was identified and authenticated by Dr. Kaushal Kumar, taxonomist and the voucher specimen number NBR- 370 is deposited in the departmental museum. The leaves were powdered and passed through a 10 – mesh sieve. The coarsely powdered material was exhaustively extracted thrice with 50 % aqueous ethanol. The extracts were filtered, pooled and concentrated at reduced temperature (5°C) on a rotary evaporator (Buchi USA) and then freeze-dried (Freezone 4.5, Labconco, USA) at high vacuum (133X10 m Bar) and at temperature -40 ±2° C (yield 9.3 %w/w). Keeping in view the % yield and activity, the 50 % ethanolic extract was taken up further detailed in toxicological and pharmacological investigations of antiulcer [16].

Experimental Animals

Male Sprague-Dawley rats (150-175g) and mice (20-30g) were obtained from National Laboratory Animal Centre (NLAC), Lucknow and housed three to a cage for the duration of the study. Animals were provided with standard rodent pellet diet (Amrut, India) and were maintained in a temperature and humidity controlled environment on a 12 –hr dark/light cycle. The food was withdrawn 24h before the experiment but water was allowed ad libitum. All studies were performed in accordance with the guide for the care and use of laboratory animals, as adopted and promulgated by the Institutional animal Care Committee, CPCSEA, India (Reg. No. 222/2000/CPCSEA).

Phytochemical screening

50 % ethanolic extract of *C. tamala* were subjected to qualitative tests for the identification of various active constituents viz. carbohydrate, glycoside, alkaloid, amino acids, flavonoids, fixed oil, tannins, gum and mucilage, phytosterols etc.

Acute oral toxicity study

Swiss albino mice were divided into eight groups of six individuals. The extract was administered orally at doses ranging from 0.1 to 2kg/gm following a standard method. A group of animals treated with 2% w/v aqueous acacia suspension (control). The animals were continuously observed for 2 hr to detect changes in the autonomic or behavioral responses. Mortality in each group was observed 24 hours followed by 7 and 14 days [17].

Anti ulcer study

A dose-response antiulcer study has been done using 50, 100 and 200 mg/kg of ethanolic extact of *C.tamala* leafs against various validated gastric ulcer models like pylorus ligation, aspirin and ethanol induced ulcers. The ethanolic extract were administered to various groups, orally, twice daily for five days and experiment were carried out on 18-24 hr fasted rats on 6th day. Ulcer were scored and analyzed as described earlier. The result indicated a dose-dependent antiulcerogenic activity in ethanolic extract of *C.tamala Linn.* (Tables). The optimal effect observed was at dose of 50 mg/kg onwards with *C.tamala Linn*. Therefore, for our further subsequent studies on other parameters of gastric secretion a dose of 50 mg/kg was selected [18].

Experimental procedure

Effect of 50 % ethanolic extract of *C.tamala* on ulcer.
Group I - Normal Control
Group II - Ulcer Control
Group III – 50 % ethanolic *C.tamala* (50mg/kg. body wt. p.o.) in ulcer rats.
Group IV - 50% ethanolic *C.tamala* (100mg/kg. body wt. p.o.) in ulcer rats.
Group V - 50% ethanolic *C.tamala* (200mg/kg. body wt. p.o.) in ulcer rats.
Group VI – Ranitidine (50mg/kg. body wt. p.o.) in ulcer rats.

50% ethanolic extract of *C.tamala* and cytoprotective drug ranitidine were administered orally twice daily at 10:00 and 16:00 hrs respectively for five days before gastric ulcers were induced. The drug samples were prepared in 1 % carboxymethyl cellulose (CMC). Control group of animals received suspension of 1 % carboxymethyl cellulose in distilled water (10ml/kg).

Pylorus ligated (PL) – induced ulcers

Gastric ulcers were produced in rats by the following method as describe earlier by (71. Sanyal 1971). Briefly, the rats were fasted for 24 hr before pylorus – ligation but water was allowed ad libitum. At the end of 24 hr starvation, rats were anaesthetized with pentobarbitone sodium (35 mg/kg). Abdomen was opened by a midline incision and a ligature was placed at the pyloric end of the stomach taking care not to exclude any blood vessels. The abdomen was then closed in two layer and rats were left in a cage with a false bottom of wide mesh wire gauze to prevent coprophagy. Water was withheld from one hour before pylorus ligation and till the end of 4 hr period when the rats were sacrificed by overdosing with ether. Immediately afterwards abdomen was again opened, cardiac end of the stomach was ligated and the stomach was taken out. The stomach was then cut open along the greater curvature and the mucosa was washed under slow running tap water. 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 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 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 (72. Sanyal 1982).

Aspirin (ASP) – induced ulcers

Aspirin was administered orally on the day of experiment at about 10 AM with the help of an orogastric tube in the form of an aqueous water suspension (200 mg/kg, p.o.) and animals were sacrificed after 4 hr of administration. The stomach was incised along with the greater curvature and examined for ulcers as described earlier [18].

Ethanol (EtOH) – induced ulcer

The gastric ulcer was induced in rats by administering Ethanol (EtOH, 100 %, 1ml/200 g, 1 hr). EtOH were administered on the day of the experiment and the animals were sacrificed by cervical dislocation and stomach was incised along with greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcer present in the glandular portion of the stomach (mm^2/rat).

Histopathological studies

Section of the stomach tissues were made, stained with Haemotoxylin and Eosin reagent and observed under low and high power objective for histopathological changes. Photomicrograph of EtOH induced rats showing hemorrhagic lesions of gastric mucosa, muscularis region has been replaced by necrotic tissue and heavy infiltration (a). There is no evidence of hemorrhagic necrosis, less infiltration and edema was visible in the gastric mucosa of rat after treatment with *C. tamala* (100 mg/kg b.w.) and EtOH (b). The stomach wall of *C. tamala* (200 mg/kg) pretreated rats showing maintenance of muscularis mucosa, regeneration of mucosa and epithelization are apparent even after exposure of EtOH (c). The Histopathological picture of Ranitidine treated rats showed normal cytoarchitecture of gastric mucosa with no pathological changes (d) [19].

Statistical analysis

All the data are presented as mean ± SEM and one-way analysis of variance (ANOVA) and Newman – Keuls Mulltiple Comparison Test was applied for determining the statistical significance between different groups.

RESULT AND DISCUSSION

Results of the preliminary phytochemical analysis carried out on the crude ethanol extract indicated the presence of carbohydrate, glycoside, alkaloid, aminoacids, flavonoids, fixed oil, tannins, gum and mucilage, phytosterols.

As shown in Table No. 1 Ethanolic extract of *C.tamala* at 50 – 200 mg/kg in PL induced ulcer model decrease the index of gastric lesion by 12.8 ± 1.81, 4.8 ± 0.94 respectively (34.74 – 75.43 % protection) in comparison to Ranitidine 3.5 ± 0.84 (82.19 %)

As shown in Table No. 2 EECT on EtOH induced ulcer model at both dose levels significantly reduced the gastric lesion by 13.33 ± 1.74, 6.16 ± 1.49, respectively (23.82 – 64.80 % protection) in comparison to Ranitidine 4.5 ± 0.84 (74.28 % protection).

As shown in Table No. 3 EECT on Aspirin induced ulcer model decrease the total ulcer index of by 15.33+ ±1.37, 3.83 ±0.94, respectively (28.69 – 82.18 % protection). Ranitidine decrease the total ulcer index of by 2.16 ± 0.30 (89.95 % protection) [20].

Figure No. 1 Microscopical examination of ethanol induced rats showing hemorrhagic lesions of gastric mucosa, muscularis region has been replaced by necrotic tissue and heavy infiltration (a).

No evidence of hemorrhagic necrosis, less infilteration and edema was visible in the gastric mucosa of rat after treatment with *C.tamala* (100mg/kg). and ethanol(b). The stomach wall of *C.tamala* (200 mg/kg) pretreated rats showing maintenance of muscularis mucosa, regeneration of mucosa and epithelization are apparent even after exposure of ethanol (c). Ranitidine treated rats showed normal cytoarchitecture of gastric mucosa with no pathological changes (d).

Table 1. Effect of *C. tamala* extract (twice daily for five days) on Pylorus ligation induced gastric ulcers

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent Protection (%)
I	Pylorus ligation	-	19.6 ±2.2	-
II	*C.tamala*	50	12.8 ±1.81[b]	34.74%
III	*C.tamala*	100	8.1 ±2.08	58.49%
IV	*C.tamala*	200	4.8 ±0.94[c]	75.43 %
V	*C.tamala*	50	3.5 ±0.84	82.19 %

Values are mean ± SEM for 6 rats [b] P<0.01 compared to respective pylorus ligated group [c]P<0.001 compared to respective pylorus ligated group.

Table 2. Effect of *C.tamala* extract (twice daily for five days) on ethanol induced gastric ulcers

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent Protection (%)
I	Ethanol	-	17.5 ± 2.60	-
II	*C.tamala*	50	13.3 ± 1.74[a]	23.82 %
III	*C.tamala*	100	8.5 ±1.99[c]	51.42 %
IV	*C.tamala*	200	6.1 ± 1.49[c]	64.80 %
V	Ranitidine	50	4.5 ± 0.84[c]	74.28 %

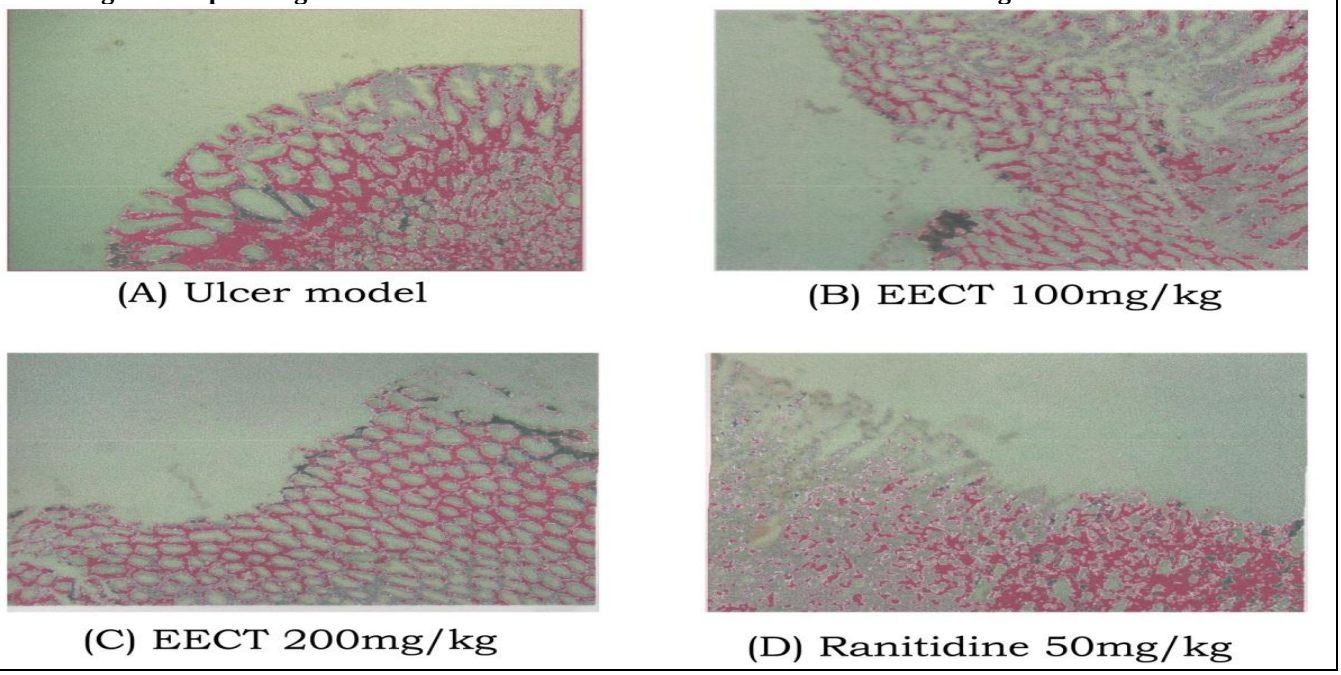
Values are mean ± SEM for 6 rats [a]P <0.05 compared to respective EtOH group [c]P< 0.001 compared to respective EtOH group.

Table 3. Effect of *C.tamala* extract (twice daily for five days) on Aspirin – induced gastric ulcers

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent Protection (%)
I	Aspirin	-	21.0 ± 1.98	-
II	*C. tamala*	50	15.33 ± 1.37[b]	28.69 %
III	*C.tamala*	100	7.33 ±0.98[c]	65.90%
IV	*C.tamala*	200	3.83 ±0.94[c]	82.18 %
V	Ranitidine	50	2.16 ± 0.30	89.95%

Values are mean ± SEM for 6 rats [b]P< 0.01 compared to respective aspirin induced group [c]P<0.001 compared to respective aspirin induced group.

Fig 1. Histopathological evaluations on the effect of C.tamala on ethanol induced gastric lesions in rats



CONCLUSION

The results showed that antiulcer activity of *Cinnamomum tamala Linn*. leaves extract was confirmed with above experimental animal studies.

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