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Anti-ulcerogenic effects of methanolic extract of unripe fruits of *Ficus racemosa* Linn.

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ABSTRACT

The anti-ulcerogenic effect of unripe fruits of *Ficus racemosa* Linn commonly known as Gular in Hindi was examined in gastric ulcer models induced by aspirin (200 mg/kg) and cold restrains stress. The 50% ehanolic extract of *Ficus racemosa* were given orally at the doses of 100 mg/kg (35.78 % and 28.82%, P<0.01), 200 mg/kg (58.33 % and 48.03%, P<0.01) and 400 mg/kg (82.84 % and 76.41%, P<0.001) and sucralfate (Standard drug) at a dose of 250mg/kg (78.43 % and 69.86%, P<0.001) for 5 days, respectively. Unripe fruits of *F. racemosa* produced significant anti-ulcer activity in all the experimental gastric ulcer models.

Key words: Anti-ulcer, Aspirin, Cold-restrain stress, *Ficus racemosa.*

INTRODUCTION

Ficus racemosa Linn (Moraceae) is commonly used in treatment of skeletal fracture in Srilanka[1]. Fruits contain Glauanol and stem bark contain tannin, leucocyanidin.[1] Methanolic extract of stem bark of *F. racemosa* is used as anti-pyretic[2] anti-tussive[3] and anti-diabetic.[4] Petroleum ether extract of leaf of this plant is used as anti-inflammatory[5] and anti-bacterial.[6] In light of the above observations the present study was undertaken to evaluate the unripe fruits of *Ficus racemosa* on experimental gastric ulceration and gastric changes in rats. Sucralfate, a non absorbable aluminium salt of sucrose octasulfate, served as reference compound. The drug sucralfate is also clinically effective in preventing stress ulceration in critically ill patients.

MATERIAL AND METHODS

Extraction

The plant materials used in this study were unripe fruits of *F. racemosa* L(Moraceae) collected from the foot hill of yercaud and identified by a botanist and voucher specimen (FRF-43) was lodged in the department museum. The unripe fruits of *F. racemosa* Linn (3 kg) chopped in to small pieces and dried under shade/ tray drier under controlled conditions and powdered coarsely. The air-dried powdered fruit of *F. racemosa* L (1000g) was first defatted with pet-ether twice and then the marc left was extracted thrice with 50% (v/v) ethanol by cold maceration for three days. The extract was separated by filtration and concentrated then dried under reduced pressure. The solid obtained was 92.0 g (yield 9.2 % w/w).

Animals used

Sprague-Dawely rats (150-180g) and albino mice (15-18g), procured from the central animal house of Central Drug Research Institute Lucknow India, were used for the study. They were kept in departmental animal house at 26 ±2 ^{0}C and relative humidity 44-56%, light and dark cycles of 10 and 14h respectively for 1 week before and during the experiments acclimatization. The animals were provided with standard rodent pellet diet (Amrut, India) and the food was withdrawn 18-th before the experiment though water was allowed

and *libitum.* All experiments were performed in the morning according to current guidelines.[7]

Acute toxicity studies

The adult male albino mice were selected for acute toxicity study. The ethanolic extract of unripe fruits of *F. racemosa* Linn was taken at various doses levels (100, 200, 400, 800, 1000, 2000 mg/kg body wt) dissolved in 1% CMC and administered 10 ml/kg orally. The animals were observed continuously for 2h and then occasionally for further 4h and finally for any mortality.

Anti-ulcer study

The animals were divided into five groups of six animals in each. First group received suspension of 1% CMC in distilled water 10 ml/kg (Ulcer control), second group received 50% ethanolic extract (100 mg/kg, p.o.), third group received (200mg/kg), fourth group received (400 mg/kg, p.o) of *F. racemosa* and fifth group received sucralfate (250 mg/kg p.o) in ulcer rats respectively. Gastric ulcers were produced in rats by Sanyal *et al.*[8] Drugs 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 % CMC. The following experimental models were used.

Aspirin (ASP)-induced ulcers[9]

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 suspension (200 mg/kg, p.o.) and animals were sacrificed after 4 h of administration. The stomach was incised along with the greater curvature and examined for ulcers as described earlier.

Cold-restraint stress (CR Stress)-induced ulcers[10]

Rats of either sex weighing 120-150 g were immobilized for 2 h at 4° C following the method of immobilization as describe earlier by Amar and Sanyal. Briefly the animals were starved for 24 h with free access to water and 60 min after receiving the corresponding treatment they were fully stretched and strapped to a wooden plank with adhesive tape after securing each limb to the plank individually. The animals were killed after 2 h and ulcer were scored as described above.

Statistical evaluation

Data are expressed as mean ± SEM (standard error of mean) for eight rats. The difference among means has been analyzed by unpaired student's t-test.

RESULTS AND DISCUSSION

Anti-ulcer study

A dose-response anti-ulcer study has been done using 100, 200 and 400 mg/kg b.w of EtOH extract of unripe fruits of *F. racemosa* Linn against various validated gastric ulcer models like aspirin and cold restraint stress -induced ulcers. The EtOH extract was administered to various groups, orally, twice daily for five days and the experiments were carried out on 18-24 h fasted rats on 6th day. Ulcer were scored and analyzed as described earlier. The result indicated a dose- dependent anti-ulcerogenic activity in EtOH extract of unripe fruits of *F. racemosa* Linn (Tables 1-2). The optimal effect observed was at the dose of 400 mg/kg onwards with *F. racemosa* Linn. Therefore, for our further subsequent studies on other parameters of gastric secretion or mucosal studies, a dose of 400 mg/kg was selected.

The aim of the present study was to assess the role of various mucosal offensive acid-pepsin and defensive mucosal factors. Attempts were made on the necessity of nontoxic, anti-ulcer compounds preferably from traditional medicinal plants such as unripe fruits of *Ficus racemosa* Linn for their protection against various experimental gastric ulcer models.

Synthetic NSAIDs like aspirin cause mucosal damage by interfering with prostaglandin synthesis, enhance acid secretion, increase back diffusion of H^+ ions, and breaking up of the mucosal barrier[11]. While ethanol perturbs superficial mucosal cells, notably mucosal mast cells to release vasoactive mediators notably LTC_4/D_4 and platelet activating factor (PAF) and histamine which damage the gastrointestinal mucosa[12]. Stress plays an important role in the causation of gastro duodenal ulceration and anti-stress drugs were found to be effective in stress-induced gastric mucosal damage. Oxidative stress has been proposed to be important etiopathological factor in genesis of peptic ulcer,

Table 1: Effect of *Ficus racemosa* Linn unripe fruit 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	200	20.4 ± 3.4	-
II	*F. racemosa* L extract	100	13.1 ± 2.8	35.78
III	*F. racemosa* L extract	200	8.5 ± 2.1[a]	58.33
IV	*F. racemosa* L extract	400	3.5 ± 2.7[b]	82.84
V	Sucralfate	250	4.4 ± 2.0[a]	78.43

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

Table 2: Effect of *Ficus racemosa* Linn unripe fruit extract (twice daily for five days) on Cold-restraint stress -induced gastric ulcers.

Group	Treatment	Dose (mg/kg)	Ulcer index (mm^2/rat)	Percent protection
I	Cold-restrain	-	22.9 ± 2.9	-
II	*F. racemosa* L extract	100	16.3 ± 2.1	28.82
III	*F. racemosa* L extract	200	11.9 ± 2.4[a]	48.03
IV	*F. racemosa* L extract	400	5.4 ± 2.1[b]	76.41
V	Sucralfate	250	6.9 ± 2.3[a]	69.86

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

while enhanced acid-pepsin appears to be directly related to Pylorus-ligated induced gastric ulcers[13]. Disturbance of gastric mucosal microcirculation, alteration in gastric secretion and abdominal gastric motility have been considered as pathogenesis mechanisms responsible for the stress-induced gastric mucosal lesions[14].

F. racemosa Linn were found to possess ulcer protective effects dose-dependently against aspirin and cold stress-induced gastric ulcer in rats. Sucralfate, a non absorbable aluminium salt of sucrose octasulfate, served as reference compound. The drug sucralfate is also clinically effective in preventing stress ulceration in critically ill patients. Sucralfate is reported to be clinically effective in healing of gastric ulcer and peptic ulcer recurrence.

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