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Research Article

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Anti gastric ulcer activity of *Ficus nervosa* bark in wistar albino rats

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ABSTRACT

The effect of chloroform, ethyl acetate and ethanolic extract of ficus nervosa bark was investigated in rats to evaluate the anti-ulcer activity by using aspirin, alcohol and pyloric ligation models experimentally induced gastric ulcer. The parameters taken to assess anti-ulcer activity were volume of gastric secretion, pH, free acidity, total acidity and ulcer index. The results indicate that the ethanolic extract 200mg/kg significantly decreases the volume of gastric acid secretion, pH, free acidity, total acidity and ulcer index with respect to standard.

Key Words: *ficus nervosa* HEYNE ex ROTH, pyloric ligation, anti-ulcer activity.

INTRODUCTION

Peptic ulcer is worldwide problem and its prevalence is quite high in India. Several field studies from different parts of our country suggest its occurrence in 3 to 10 per thousand populations. The exact cause of peptic ulcer is not known, the disease results in chronic suffering, loss of working hours and occasional fatality. Smoking, alcoholism and spices add to the severity of the disease that often precipitate serious complication of ulcer [1]. Indigenous drugs possessing fewer side effects should be looked for as a better alternative for the treatment of peptic ulcer. There is evidence concerning the participation of reactive oxygen species in etiology and pathophysiologhy of human disease, such as neurodegenerative disorders such as gastro inflammation and gastric ulcer [2].

Herbal medicine is fast emerging as an alternative treatment to available synthetic drugs for treatment of ulcer possibly due to lower costs, availability, fewer adverse effects and perceived effectiveness. In the present study we selected a plant namely *ficus nervosa (*moraceae*).* It is an monoecious evergreen medium sized trees used traditionally for its curative property in treating diabetes, rheumatism and ulcer disorders.[3] From the literature survey, *ficus nervosa* roots have been reported to contain several secondary metabolites like flavonids ,coumarin ,flavones ,steroids, triterpenoids which also possesses the antimycobacterial activities[4].However, the chemical constituents and biological activities of *ficus nervosa* bark have never been investigated, thus the present study was initiated to evaluate anti ulcer activity of various extract of stem bark of *ficus nervosa*.

EXPERIMENTAL SECTION

Material and Methods [5]

The plant of *ficus nervosa* HEYNE ex ROTH collected from the chittoor district was authenticated by Dr. K. Madhava chetty, Ph.D., Department of botany, S.V University, Tirupathi. Voucher Specimen no-0603. The stem bark of *ficus nervosa* was shade dried after collection of 15 days and was coarsely powdered. The powdered bark was defatted with petroleum ether and then subjected to continuous hot extraction in soxhlet apparatus with chloroform, ethyl acetate, and ethanol. The extract was filtered through a cotton plug, followed by whatmann filter paper (no.1). The extract was evaporated under reduced pressure using rotovac evaporator at a low temperature (40-60^{o}c)

Phytochemical studies [6]:

The various extract of *ficus nervosa* were subjected to preliminary phytochemicals and it revealed the presence of alkaloids, flavoinds, terpenoids, steroids ,tannins and carbohydrates.

Animals

Wistar Albino rats (150-200mg) of either sex were used in this investigation. They were maintained at standard housing condition and fed with commercial diet (Hindustan lever ltd., Bangalore) and provided with water *ad libitum* during the experiments. The Institutional Animal Ethical Committee permitted the study.

Acute toxicity studies

Acute toxicity study was performed for various extracts of *ficus nervosa* according to the acute toxic classic methods as per OECD guidelines [7]. The animals were kept fasting for overnight providing only water, after which the various extracts were administrated orally at the dose of 2000mg/kg was prepared by dissolving the extract in distilled water and the concentration was adjusted in such a way that it did not exceed 1ml/100g of the rat. The extract was then administrated (p.o) and animals were observed for behavioral changes, any toxicity and mortality up to 48 hrs.

Anti-ulcer activity

Pyloric ligation model [8]

The albino rats of either sex weighing between 150-200g were divided into 5 groups of 6 animals. The animals were deprived of food for 24 hours, before the commencement of experiments, but water allowed at *ad libitum*. After the fasting period the rats were anaesthetized with light ether. The abdomen was opened and the pyloric end was ligated with a thread [9]. All the samples were given 60 minutes prior to pyloric ligation [10].

Group-I received distilled water (1ml/kg, p.o) act as a control, Group-II received Ranitidine (30 mg/kg, p.o.) act as a standard, Group-III received chloroform extracts (100&200 mg/kg, p.o) and Group-IV received ethyl acetate extract (100&200mg/kg, p.o), Group-V received ethanolic extract (100&200mg/kg, p.o).

After 4 hours of pyloric ligation all the animals were sacrificed to observe gastric lesions. The gastric juice was collected and centrifuged at 1000 rpm for 10 minutes. The volume of gastric juice (ml) as well as pH of gastric juice was noted [11]. Then the gastric juice was subjected to biochemical estimation [12]. The gastric ulcer score was recorded according to the method described by Aguwa and Ukwe (1997) [13].

Gastric content were assayed for total acidity by titration against 0.01N NaOH using phenolphthalein as indicator. The volume of gastric content was measured and the total acidity and free acidity were estimated [14]. The data concerning the pH, acid secretion were analyzed by One-Way analysis of variance (ANOVA) and followed by student't' test were show in Table-1[15].

Aspirin induced gastric ulcer[16]:

In the aspirin induced ulcer experiments, five groups of albino rats with each group consisting of six animals were used. The first group served as a control group, the second group served as standard and the third, fourth and fifth groups were treated respectively with chloroform, ethyl acetate and ethanolic extract of *ficus nervosa* (100mg/ 200mg), orally for 8 days. Control animals received normal saline (2ml/kg) for 8 days. After 8 days of treatment .animals were fasted for 24 hrs. ulcer was produced by administration of aqueous suspension of aspirin (a dose of

200 mg/kg orally) on the day of sacrifice .The animals were sacrified 4h later and stomach was opened to calculate the ulcer index by kunchandy method[17]

Alcohol induced gastric ulcer:
Albino rats were randomly divided in to five groups and fasted for 24 hrs with free access to water, animals were given vehicle, chloroform, ethyl acetate and ethanolic extract of the *ficus nervosa* at a dose of 100and 200 mg/kg or ranitidine (20mg/kg) orally. One hour later ,1ml of 80% ethanol administrated orally to each animal[18], animals were sacrified by cervical dislocation, one hour after ethanol administration ,stomachs were isolated and cut open along the greater curvature and pinned on a soft board. The length of each gastric lesion was measured and the lesion index was expressed as sum of the length of the entire lesion in mm.

RESULTS

The preliminary chemical test reveals the presence of alkaloids, flavonids, terpenoids, steroids, tannins, carbohydrates in *ficus nervosa*. Acute toxicity studies of the various extracts of the *ficus nervosa* did not exhibit any signs of toxicity up to 2g/kg body weight. Since there was no mortality of the animals found at high dose. Hence 100 and 200 mg/kg dose of the extract selected for evaluations of anti-ulcer activity.

Pylorus ligation induced ulcer
The results of oral administration of chloroform, ethyl acetate and ethanolic extracts of the *ficus nervosa* at 100 and 200 mg/kg b.w on different chemical parameters in rats were represented in Table-1.

Table-1: Effect of various extracts of *ficus nervosa* bark against pylorus ligation induced gastric ulcer in rats

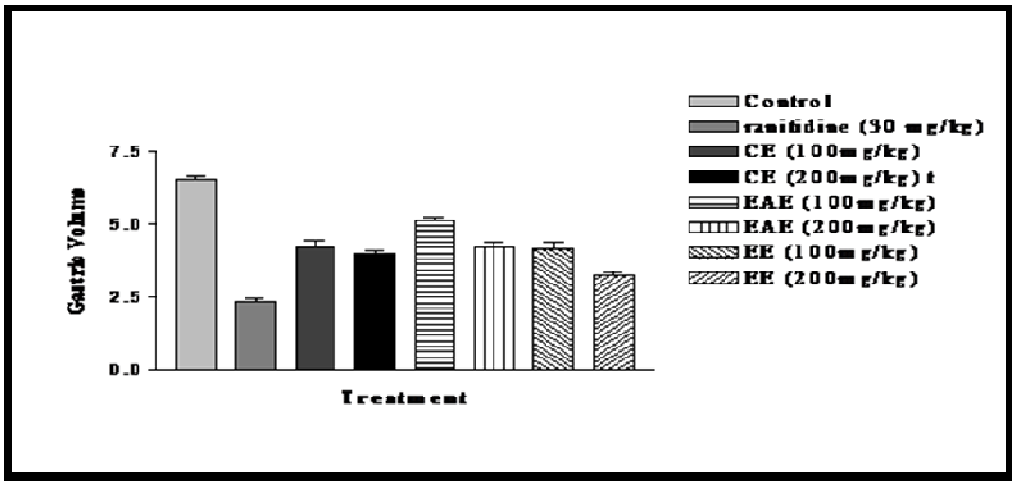
Group	Treatment and Dose mg/Kg	Gastric volume (ml)	pH	Free acidity (mEq/l)	Total acidity (mEq/l)	Ulcer score	% Inhibition of ulcer
I	Control distilled water ml/kg	6.52±0.12	1.85±0.14	25.91±0.06	58.60±0.30	3.54±0.56	_
II	Standard ranitidine 30 mg/kg p.o	2.36±0.07	4.56±0.12	9.45±0.02	21.76±0.24	0.74±0.12	82.80***
III	Chloroform extract 100mg/kg p.o	4.23±0.23	3.25±0.16	18.65±0.04	48.56±0.65	2.68±0.36	32.40*
	Chloroform extract 200 mg/kg p.o	3.96±0.12	3.86±0.18	17.24±0.02	45.34±0.58	2.48±0.42	38.58*
IV	Ethyl acetate extract 100mg/kg p.o	5.12±0.12	2.98±0.15	19.67±0.08	44.45±0.34	2.84±0.56	34.68*
	Ethyl actetate extract 200 mg/kg p.o	4.21±0.16	3.30±0.16	18.43±0.05	50.24±0.06	1.84±0.32	57.42**
V	Ethanolic extract 100 mg/kg p.o	4.15±0.21	3.24±0.14	16.47±0.08	38.65±0.08	2.04±0.14	70.24**
	Ethanolic extract 200 mg/kg p.o	3.24±0.14	3.96±0.18	14.32±0.07	30.24±0.21	1.54±0.16	78.34***

Results are mean ±S.E.M .(n=6) Statistical comparison was performed by using ANOVA coupled with student 't' test. P<0.05, **P<0.01,***P<0.001 were consider statistically significant when compared to control group.*

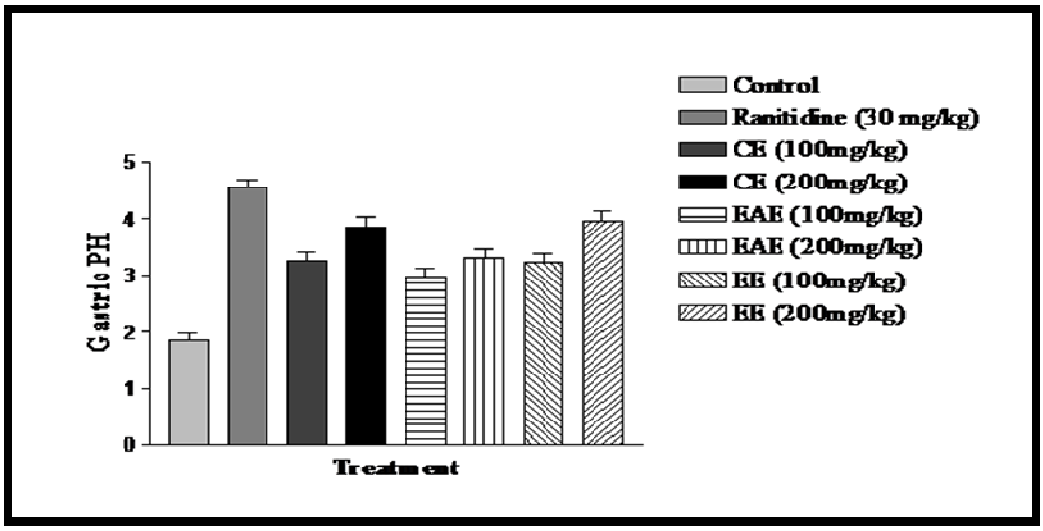
All the extracts of *ficus nervosa* in different doses produced a reduction in the ulcer index, gastric volume, free acidity, total acidity and raised gastric pH significantly in comparison with control group. Ranitidine standard drug produced significant reduction gastric ulcer and total acid output as compared to control group. But ethanolic extract 200mg/kg showed (Fig.1) almost similar effects as that of ranitidine (30mg/kg) in reducing the gastric volume.

Compared to control group the entire test showed (Fig.2) elevation in pH indicating their capacity to reduced the acidity of the gastric juice. The ethanolic extract at 200mg/kg indicated almost equipotent effect as that of ranitidine.

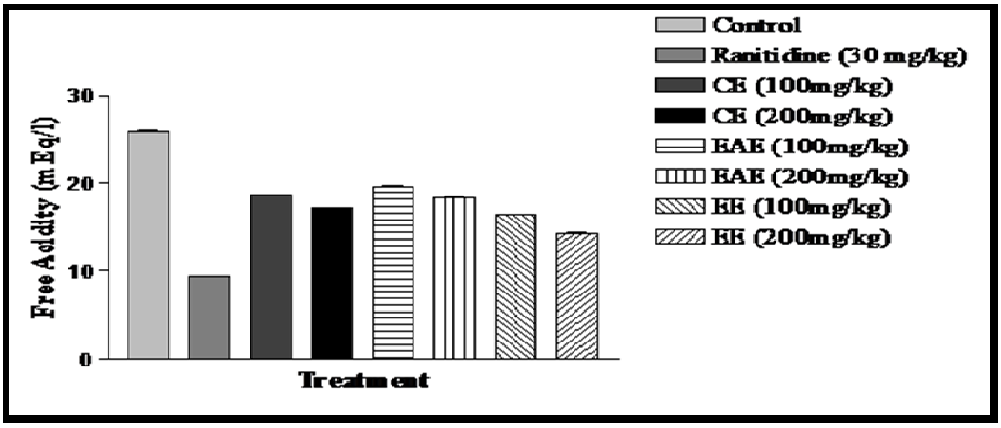
Gastric free acidity is increased in control animals due to pylorus ligation. Various extracts of *ficus nervosa* at 200 mg/kg decreased the gastric free acidity respectively. When compared to ranitidine effect, ethanolic extract showed (Fig. 3) significant effect in reducing the gastric free acidity.



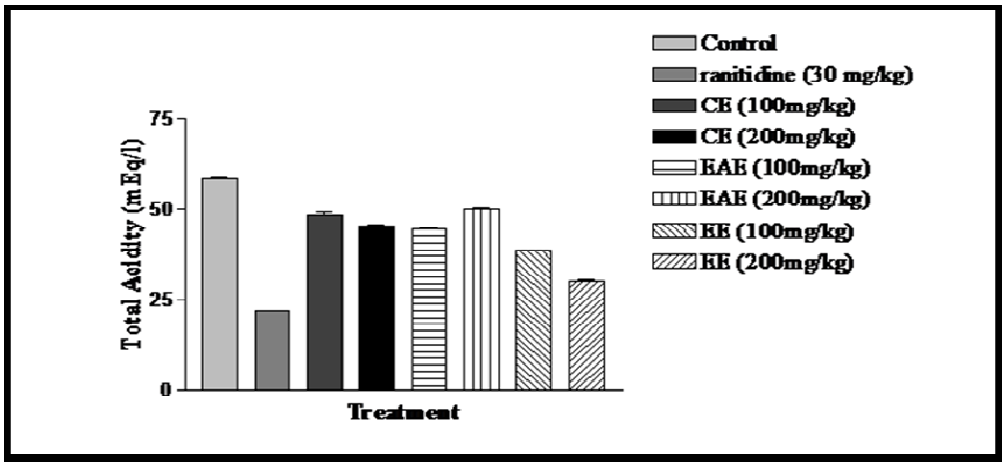
(Fig.1) Effect of various extract of *Ficus nervosa* on Gastric Volume



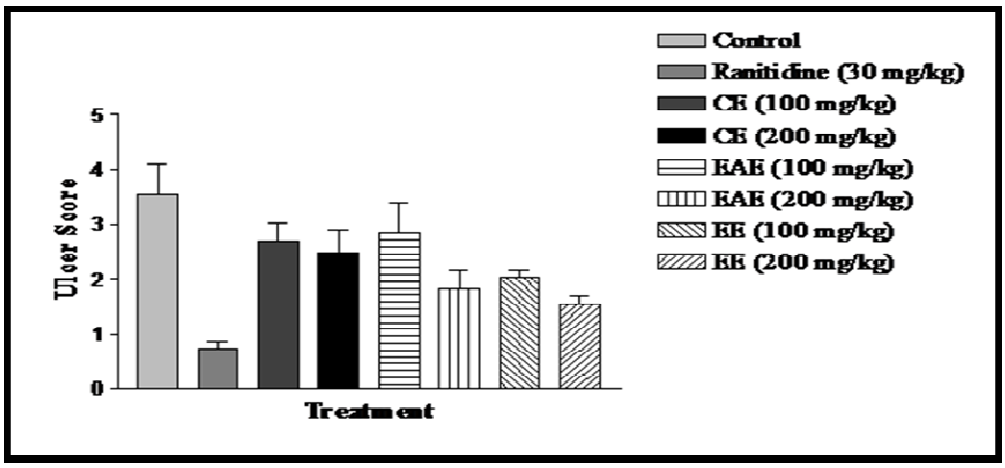
(Fig.2) Effect of various extract of *Ficus nervosa* on Gastric PH



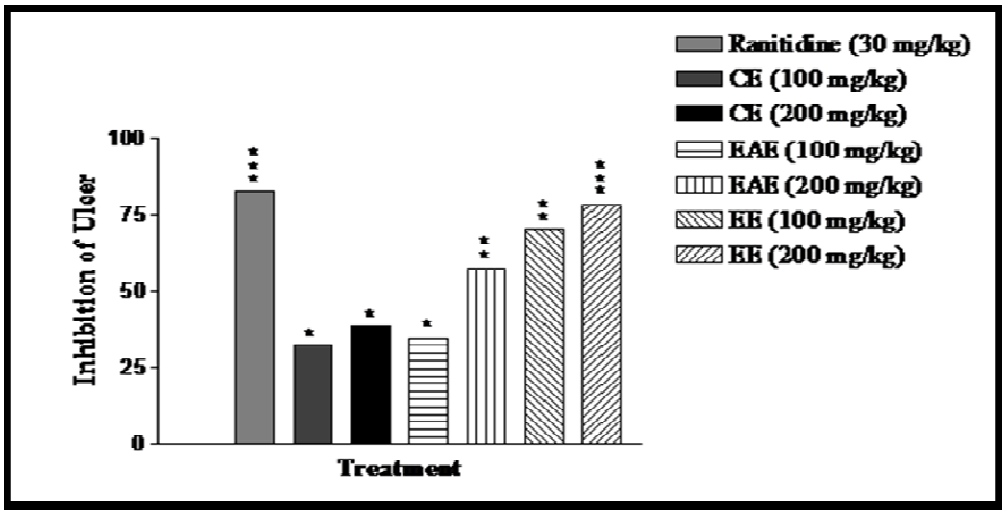
(Fig.3) Effect of various extract of *Ficus nervosa* on Free Acidity



(Fig.4) Effect of various extract of *Ficus nervosa* on Total Acidity



(Fig.5) Effect of various extract of *Ficus nervosa* on Ulcer Score

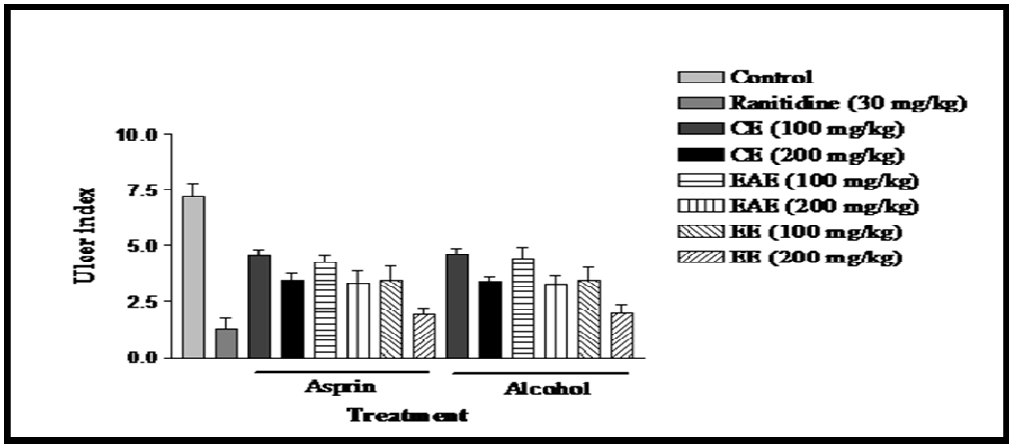


(Fig.6) Effect of various extract of *Ficus nervosa* on % Inhibition of Ulcer

Total acidity showed (Fig. 4) decrease in various extract when compared to control. All the extract at 200 mg/kg reduced the mean ulcer score respectively (Fig. 5) and percentage curative ratio of ethanolic extract at 200 mg/kg was almost comparable to that of standard ranitidine (Fig.6).

Aspirin induced ulcer

Table-2 summarizes the results obtained in the experimental model of aspirin induced gastric ulceration in rats. The ethanolic extract of *ficus nervosa* was found to possess remarkable ulcer protective properties at 100 &200 mg/kg when compare to other two extracts(Fig.7). The maximum effect of ulcer protection (45.65%),(48.46%)& (70.46%) were produced at 200 mg/kg for chloroform, ethyl acetate, and ethanolic extracts and the standard drug ranitidine 20 mg/kg gave 82.68% of ulcer protection.



(Fig. 7) Effect of various extract of *Ficus nervosa* against Aspirin and Alcohol induced gastric ulcer in rat

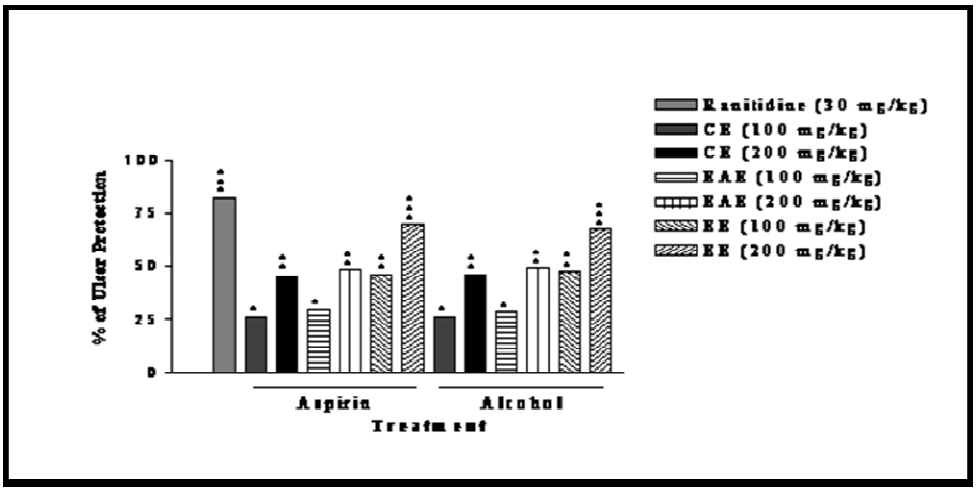
Table-2 Effect of various extracts of *ficus nervosa* bark against aspirin and alcohol induced gastric ulcer in rats

Treatment	Dose(mg/kg)p.o	Aspirin		Alcohol	
		Ulcer index	% of ulcer protection	Ulcer index	% of ulcer protection
Control (normal saline)	2 ml/kg	7.2±0.60	-	7.2±0.60	-
Standard (Ranitidine)	20mg/kg	1.30±0.43	82.68***	1.30±0.43	82.68***
Chloroform extract	100mg/kg	4.56±0.29	26.23*	4.62±0.26	26.54*
	200mg/kg	3.45±0.32	45.65**	3.41±0.23	46.24**
Ethyl acetate extract	100mg/kg	4.24±0.32	29.32*	4.42±0.52	28.65*
	200mg/kg	3.32±0.56	48.46**	3.26±0.42	49.47**
Ethanolic extract	100mg/kg	3.46±0.65	46.54**	3.49±0.53	47.36**
	200mg/kg	1.92±0.32	70.46***	1.98±0.38	67.42***

Results are mean±S.E.M.(n=6) Statistical comparison was performed by using ANOVA coupled with student 't' test. P<0.05, **P<0.01,***P<0.001 were consider statistically significant when compared to control group.*

Alcohol induced ulcer

Pretreatment of rats with *ficus nervosa* extracts produced a dose dependent protection in the ethanol induced ulceration model as compared to control group. The maximum effect of ulcer protection (46.24%),(49.47%),(67.42%) were produced at 200mg/kg for chloroform, ethyl acetate and ethanolic extracts(Fig.8). However the protection was statistically significant reduced the severity of ulcer and caused a significant reduction of ulcer index in this model. ranitidine produced significant gastric ulcer protection as compared to control group.



(Fig. 8) Effect of various extract of *Ficus nervosa* against Aspirin and Alcohol induced gastric ulcer in rat

DISCUSSION

The anti ulcer activity of *ficus nervosa* was evaluated by pylorus ligation, aspirin, alcohol induced ulcer models. These models represent some of the most common causes of gastric ulcers in human. So it has been proposed that in pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for induction of ulceration [19].The anti ulcer activity of *ficus nervosa* extracts in pylorus ligation model is evident from its significant reduction in gastric volume total acidity, free acidity, ulcer index and increase in pH of gastric juice. NSAIDs like aspirin causes gastric mucosal damage by decreasing prostaglandin levels through inhibition of PG synthesis. [20] Ethanolic extract of the plant of *ficus nervosa* was significantly effective in protecting gastric mucosa against aspirin induced ulcers. Ethanol induced gastric injury is associated with significant production of oxygen free radicals leading to increased lipid peroxidation ,which cause damage to cell and cell membrane[21]. The various extracts of *ficus nervosa* has significantly protected the gastric mucosa against ethanol challenge as shown by reduced values of lesion index as compared to control group suggesting its potent cytoprotective effect. Preliminary phytochemical studies revealed the presence of flavonoids. So the possible mechanism of antiulcer action of *ficus nervosa* bark may be due to its flavonoid content. In this study we observed that *ficus nervosa* provides significant anti ulcer activity against gastric ulcer in rats.

CONCLUSION

On the basis of the present results, it can be concluded that the anti ulcer activity elucidated by *ficus nervosa* could be mainly due to the modulation of defensive factors through an improvement of gastric cytoprotection and partly due to acid inhibition.

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