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Full Length Research Paper

Anti-ulcerogenic evaluation of root extract of *Ficus hispida* Linn. in aspirin ulcerated rats

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The present study was designed to investigate the anti-ulcer efficacy of methanolic root extract of the *Ficus hispida* Linn. (FH), which was known to possess various therapeutic properties. The reason for the study was that the known non-steroidal anti-inflammatory drugs (NSAIDs) were full of side effects especially ulceration causes Gastric ulceration an economic loss and a source of welfare concern worldwide. There are 350,000 to 500,000 new cases per year and more than one million are ulcer-related hospitalizations. We found that FH decreased the incidence of ulcers and also enhanced the healing of ulcers. Methanolic extract of FH at doses 200 and 400 mg/kg was found to be effective by 63.8 and 68.44% respectively in aspirin (ASP) induced ulcer model and significantly reduced free and total acidity. It was observed that anti-ulcer effect of FH might be due to its cytoprotective effect rather than antisecretory activity. Conclusively, FH was found to possess potent anti-ulcerogenic as well as ulcer-healing properties and could act as a potent therapeutic agent against peptic ulcer disease.

Key words: *Ficus hispida* Linn., peptic ulcer, aspirin, non-steroidal anti-inflammatory drugs.

INTRODUCTION

Ficus hispida (FH) Linn. belongs to the family Moraceae moderate sized tree, up to the level of 3.0 m, with spreading branches and many aerial roots. It is widely distributed throughout India, Srilanka, Myanmar, Southern region of the Republic of China, New Guinea, Australia and Andaman Islands in damp localities, as well as grows in secondary forests, open lands and river banks up to 1200 m in altitude (Ripu and Bussmann, 2006). FH is used by the maaiba (indigenous medicine - man of Manipur) as an indigenous traditional medicine (Manandhar, 1995). All parts of the plant have been reported to be bitter, cooling, astringent, antidysentric, psoriasis, anemia, piles, jaundice, and hemorrhage (Nadkarni, 1976; Rastogi and Mehrotra, 1993).

The fruit acts as a coolant and tonic. The juice obtained from the fig is taken with jaggery as a mild purgative. A mixture of honey and its juice is a good antihemorrhage (Sergio et al., 2002) the root and leaves are of particular interest from a medicinal point of view as an antidiarrhoeal (Subhash and Mandal, 2002), antidiabetic (Ghosh et al., 2004), hepatoprotective (Jung et al., 2008), antibacterial (Kone et al., 2004) and as cardio protective (Shanmugarajan and Arunsunda, 2008) among others. The current study was undertaken to evaluate the anti-ulcer activity of FH methanolic extract by aspirin induced gastric ulcer, till now no pharmacological evaluation has been done on FH especially in root for its anti-ulcer activity. This prompted us to pursue the activity and examine for their efficacy as well as to determine their possible mechanism of action.

MATERIALS AND METHODS

Plant material

The fresh roots of FH were collected from (Peranakkavur, Changlepet and Tamilnadu, India) Western Ghats of South India during May 2008. The plant was identified and authenticated by Dr. G. V. S. Murthy, Joint Director, Botanical Survey of India, Southern Circle, Coimbatore (BSI/SC/5/23/08-09/Tech-738) Tamil Nadu, India. The specimen voucher was deposited in the Department of Pharmacology and Toxicology, C. L. Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India

Preparation of the methanolic extract of FH

The fresh root of FH was collected and washed with running water.

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It was shade dried at room temperature and 1 kg of the dried root was made into coarse powder. The powder was passed through a 60 No mesh sieve. The ground power was extracted with methanol in water bath at room temperature. The solvent was then removed by filtration and fresh solvent was added to the plant material. The extract process was twice repeated. The combined filtrates were then evaporated under reduced pressure to give a dark green viscous mass. The extract was stored at 0 - 4℃. The percentage yield was 16% w/w ± 2%.

Phytochemical screening

The freshly prepared root extract of FH was qualitatively tested for the presence of chemical constituents. Phytochemical screening of the extract was performed using the following reagents and chemicals: alkaloids with Mayer's, Hager's and Dragendorffs reagent; flavonoids with sodium acetate, ferric chloride, amyl alcohol; phenolic compounds and tannins with lead acetate and gelatin; carbohydrate with Molish's, Fehling's and Benedict's reagent; proteins and amino acids with Millon's, Biuret, and xanthoprotein test. Saponin was tested using hemolytic method; gum was tested using Molishs reagent and Ruthenium red; coumarin by 10% sodium hydroxide and quinones by concentrated sulphuric acid. These were identified by characteristic color changes using standard procedures (Trease and Evans WC, 1989).

Animals

Swiss albino rats of either sex, weighing (180 - 200 g) were obtained from animal house of C. L. Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India. Animals were kept in raised mesh bottom cages to prevent coprophagy. The animals were maintained in colony cages at 25 ± 2℃, relative humidity 50-55% maintained under 12:12 h light and dark cycle. The animals were fed with standard animal feed (Hindustan Lever Ltd. Bangalore, India) and water *ad libitum*.

All the animals were acclimatized to the laboratory conditions prior to experimentation. All the experiments were conducted between 10.00 and 17.00 h and were in accordance with the ethical guidelines of the International Association for Study of Pain (Zimmerman, 1983). All experiments were carried out according to the guidelines for care and use of experimental animals and approved by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). The study was approved by the Institutional Animal Ethical Committee (Ref No: IAEC 12/15-CLBMCP, dated 10-10-2008).

Acute toxicity study

Acute toxicity study was performed for the extracts to ascertain safe dose by acute oral toxic class method of Organization of Economic Co-operation and Development, as per 423 guidelines (OECD) (Donald and Ecobichon, 1997).

Treatment schedule

Swiss albino rats of either sex were divided into four groups, each group consisted of six animals. All groups of animals received treatments as shown below along with 200 mg/kg of aspirin once daily for 3 days. Group 1 received 1.0 ml/kg p.o 1% SCMC sodium carboxy methyl cellulose (MERK, India) as vehicle control; Group 2 received 200 mg/kg, p.o ranitidine(Sigma Chemical, Bangalore ,India standard, Group 3 received 200 mg/kg, p.o methanolic root extract of FH, Group 4 received 400 mg/kg, p.o methanolic extract of FH.

Aspirin induced gastric ulcer in rats

The modified method of Geol et al. (1985) was used for the production of experimental gastric ulceration, that is, in rats, by administering aspirin (200 mg/kg) suspended in 1% sodium carboxymethyl cellulose. The aqueous suspension of aspirin was administered with the help of a round tip cannula at 12.00 h. Methanolic extracts of FH, (200 and 400 mg/kg), were administered orally 3 h prior to and after the aspirin treatment. This regimen was continued for 3 consecutive days, following 36 h fasting. Four hours after the aspirin administration the animals were sacrificed by decapitation. The stomach was opened and the percentage inhibition of ulcer was determined (Ganguly and Bhatnagar, 1973). Mean ulcer score for each animal was expressed as ulcer index. The maximum length of each lesion was determined and the sum of the lengths of all lesions in each stomach was expressed as the ulcer index (Okabe et al., 1978; West, 1982).

Percent inhibition

% inhibition = Ulcer index (vehicle) - Ulcer index (drug) × 100

The curative ratio (C.R.) was calculated according to the formula:

(Control ulcer index - treated ulcer index)/ (control ulcer index) × 100.

The number of ulcers per stomach was recorded and the percent of ulcer incidence of each group as compared to the control was calculated (Sanyal et al., 1982). The gastric juice was titrated against 0.01 N sodium hydroxide using Topfer's reagent as indicator to find out the free acidity and total acidity (Kulkarni, 1999) as per (Figure 1)

Statistical analysis

All values were expressed as mean ± S.E.M. Data of ulcer index was analyzed by non-parametric ANOVA followed by Dunnett's multiple comparison test and other data was evaluated by one-way ANOVA followed by Dunnett's multiple comparison test using Graph Pad PRISM software. P-value < 0.05 was considered significant.

RESULTS

The screening results were as follows: alkaloids + ve; carbohydrates +ve; proteins and amino acids +ve; steroids - ve; serols +ve; phenols +ve; flavonoids +ve; gums and mucilage +ve; glycosides + ve; saponins +ve; terpenes +ve and tannins -ve,

Where +ve and -ve indicated the presence and absence of compounds. In the aspirin induced ulcer model, it was observed that the treatment with methanolic root extract of FH (200 and 400 mg/kg) and ranitidine (200 mg/kg) significantly reduced the lesion index, the total, free acidity as per (Table 1) and the percentage of ulceration, in comparison with negative control group ($p < 0.05$). The percentages of inhibition of ulcers were 68.72%, for the test groups with 200 mg/kg of FH methanolic root extract and 62.13% for 400 mg/kg FH

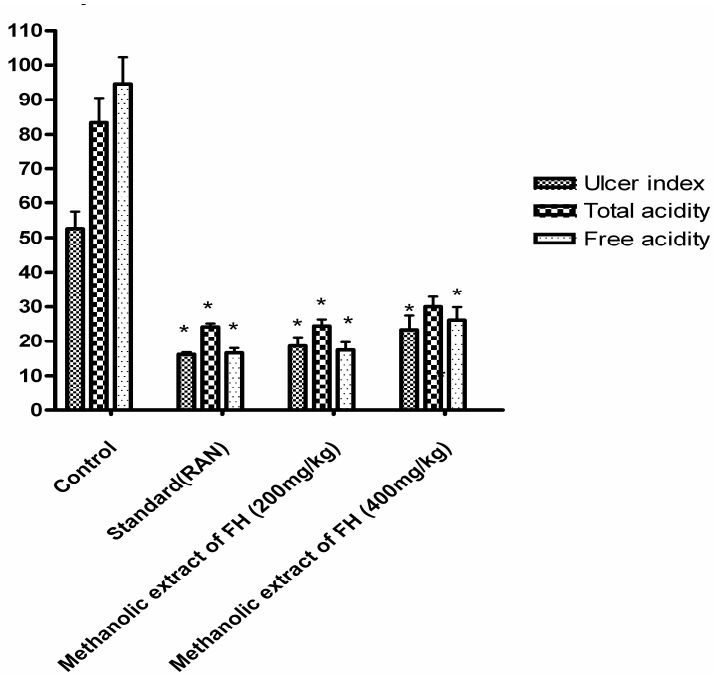

Figure 1. Effect of FH on ulcer index (UI), Free and Total acidity and inhibition of ulcers in Aspirin induced ulcer model. The results are mean ± S.E.M. for six rats. Statistical compa-rison was performed using ANOVA followed by the Dunnet's test. *p < 0.05 in comparison with the control group.

Table 1. Effect of methanolic root extract of FH on ulcer index, total acidity, and free acidity aspirin induced gastric ulcer in rats.

Treatment (mg/kg)	ulcer index	Total acidity	Free acidity
Vehicle control (1% SCMC)	52.6 ± 4.9	83.4 ± 7.1	94.6 ± 7.6
Ranitidine (200 mg/kg)	16.2* ± 0.6	24.2* ± 0.9	17.5* ± 2.2
Methanolic root extract of FH (200 mg/kg)	18.6* ± 2.5	24.4* ± 1.9	16.6* ± 1.4
Methanolic root extract of FH (400 mg/kg)	23.3* ± 4.1	30.0* ± 2.9	26.1 ± 3.8

Each value is the mean ± S.E.M. of six determinations. *P < 0.05. Dunnet test as compared to control.

Table 2. Effect of methanolic root extract of FH against aspirin induced gastric lesion in rats.

Treatment Dose (mg/kg)	Mean lesion index	% Ulcer inhibition
Vehicle control 1% SCMC	52.6±4.1	-
Ranitidine 200 mg/kg	14.2*±1.9	73.0
Methanolic extract of FH 200 mg/kg	19.1*±3.9	63.68
Methanolic extract of FH 400 mg/kg	16.6*±0.9	68.44

Each value is the mean ± S.E.M. of six determinations. *P < 0.05. Dunnet test as compared to control.

methanolic root extract when compared with standard group as per (Table 2).

DISCUSSION

Peptic ulcer is now believed to be due to an imbalance between the acids and pepsin and defensive factors collectively called the mucosal barrier (Baron et al., 1980). Gastric ulcer is usually due to weakening of the gastric mucosa, and duodenal ulcer due to the dominance of acid and pepsin. Risk of ulcerogenesis is now greatly enhanced due to socio-economic problems and exposure of man to many noxious agents and chemicals (Croft, 1997).

1977). Ulcer is the fourth largest disease in Asia. Many drugs available on the market greatly reduce the morbidity and mortality, but may also produce adverse reactions like gynaecomastia (Ariypshi et al., 1986) and also suffer from high recurrence rates.

Aspirin decreased the concentrations of all the individual carbohydrates and also the carbohydrate to protein ratio; however a similar decrease in carbohydrate/protein ratio and of individual carbohydrates has been earlier reported in the non-dialyzable and lyophilized fractions of the mucus in aspirin-treated dogs (Menguy and Masters, 1965). These results tend to confirm that aspirin-like drugs cause ulceration by affecting the mucosal barrier and the carbohydrate/protein ratio of the gastric juice is a good index of the mucus barrier.

The methanolic extract of FH at doses 200 and 400 mg/kg produced a significant gastric ulcer when compared with the negative control (aspirin) and with the ranitidine (standard).

Conclusion

In conclusion, it is demonstrated that the methanolic extract of FH was undoubtedly an anti-ulcer molecule but by multiple mechanisms. The anti-ulcer activity data of FH signified that it might be either by increasing the gastric mucosal resistance, local synthesis of cytoprotective prostaglandins synthesis (Tseng et al., 1992). Hence, it was right to state here that FH, which was used as a therapeutic agent had an anti-ulcer potential. Further work for its specific anti-ulcer mechanism is in progress.

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