



ANTI-ULCER ACTIVITY OF *FICUS RELIGIOSA* L. LEAVES ON EXPERIMENTAL ANIMALS

Hemant Kumar^{1*}, Shrish Kumar Srivastava², Chandana V. Rao, Sanjay Yadav³

1. National and Botanical Research Institute, Lucknow - 226001, India.

2. The Pharmaceutical College, Barpali, Orissa-768029, India.

3. Saroj Institute of Technology and Management, Lucknow - 226001, India.

*Corresponding author's E-mail: hemantch17@gmail.com

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ABSTRACT

Ficus religiosa is being used in Ayurvedic and Malay traditional medicine for the treatment of various diseases including gastric ulcer. Considering the above claims, the present work was undertaken to validate the anti-ulcer potential of the ethanol extract of leaves of *Ficus religiosa* against *in vivo* aspirin induced ulcer and pylorus ligation assays. Gastric ulcers induced in Swiss albino rats by oral administration of aspirin suspension and ligate the pylorus part of stomach. The antiulcer activity was examined by determining and comparing the ulcer index in the test drug groups with that of the vehicle control and standards. Therefore all models showed significant anti-ulcer property in a dose dependent manner. The parameters taken to assess antiulcer activity were volume of gastric juice, free acidity, total acidity and ulcer index. The results indicated that ethanolic extract significantly ($p < 0.001$) decreased the volume of gastric acid secretions, free acidity and total acidity and ulcer index.

Keywords: *Ficus religiosa*, Pylorus ligation, Aspirin, Acidity, Ulcer index.

INTRODUCTION

Natural product is a source for bioactive compounds and has potential for developing some novel therapeutic agent. Over the last decade there has been a growing interest in drugs of plant origin and such drugs formed an important class for disease control.¹

Plants have played a significant role in maintaining human health and improving the quality of human life for thousands of years and have served humans well as valuable components of medicines, seasonings, beverages, cosmetics and dyes. Herbal medicine is based on the premise that plants contain natural substances that can promote health and alleviate illness². This research emphasizes the traditional use and clinical potentials of *F. religiosa*. Through which the authors hope to attract the attention of natural product researchers throughout world on the explored potential of *F. religiosa*. *F. religiosa* Linn (Moraceae) commonly known as 'Peepal tree' is a large widely branched tree with leathery, heart shaped, long tipped leaves on long slender petioles and purple fruits growing in pairs. The tree is regarded as a sacred tree to both Hindus as well as Buddhists. It has got mythological, religious and medicinal importance in Indian culture since ancient times. *F. religiosa* Linn (Moraceae) commonly known as 'Peepal tree' is a large widely branched tree with leathery, heart-shaped, long-tipped leaves on long slender petioles and purple fruits growing in pairs.³

F. religiosa belongs to a class of drugs called rasayana. Rasayana are rejuvenators, antioxidants and relieve stress in the body^{4,5} and having Anthelmintic activity⁶, Antibacterial activity⁷, Antioxidant activity⁸, Wound-healing activity⁹, Anticonvulsant activity¹⁰,

Hypoglycemic activity¹¹, Hypolipidemic activity¹² and Immunomodulatory activity¹³. The leaves reported antivenom activity and regulates the menstrual cycle^{14, 15}. Leaves and bark are astringent and laxative and are employed together to relieve diarrhea and dysentery and also to help reduce bleeding. Leaves and fruits contain carbohydrate, protein, lipid, calcium, sodium, potassium, and phosphorus¹⁶. Leaves yield campesterol, stigmasterol, isofucosterol, α -amyrin, lupeol, tannic acid, arginine, serine, aspartic acid, glycine, threonine, alanine, proline, tryptophan, tyrosine¹⁷⁻¹⁹. The extracts of *F. religiosa* were found to be active against *Aspergillus niger* and *Penicillium notatum*.

MATERIALS AND METHODS

Collection of plant material

The leaves plant of *Ficus religiosa* were collected from Botanical Garden of National Botanical Research Institute, Lucknow, India in month of October 2010. The plant materials were authenticated by Dr Tariq Husain, Head & Scientist, Biodiversity & Angiosperm Taxonomy at National Botanical Research Institute; Lucknow and voucher specimens (98145) were deposited in the departmental herbarium of National Botanical Research Institute, Lucknow, India for future reference.

Extraction of *F. religiosa*

Initially these leaves were washed with fresh water to remove adhering dirt and foreign particles and dried at 35 -40°C in an oven. The dried leaves were crushed and grinded to get powder and weighed. The weighed powder was then placed with ethanolic solution in a cylinder. 500g of *Ficus religiosa* leaves powder in 1.0 liter of ethanolic solution were macerated for 7 days. The



menstrum was removed and concentrated by vacuum distillation. Again the crude material was allowed to undergo maceration for 4 days followed by 2 days for complete extraction.²⁰ The menstrum was collected and concentrated using Rotary evaporator at 50°C.²¹ This mixture was cooled and filtered by Buchner funnel and filter paper and then air dried in an evaporating dish till constant weight was obtained.

Animals

Swiss albino rats weighing (150-200 gm) were procured from National Botanical Research Institute (Lucknow). They were housed in the departmental animal house under standard conditions (26 ± 2°C and relative humidity 30-35%) in 12 hours light and 12 hours dark cycle respectively for 1 week before and during the experiments. Animals were provided with standard rodent pellet diet and had free excess to water. The composition of diet is 10% protein, 4% arachis oil, 1% fibers, 1% calcium, 1000 IU/gm vitamin A and 500 IU/gm vitamin D.

Experimental Procedure

Animals were divided into four groups (n=6). Group-I received carboxymethyl cellulose 1% (10ml/kg,p.o.) that served as control, group-II received ranitidine orally (50 mg/kg), group-III, IV received ethanolic extracts (250mg/kg, 500mg/kg) and sucralfate in case of aspirin model.

Pharmacological Screening of Plant Extract

Pylorus Ligation Induced Ulcer

Gastric ulcers were produced in rats by following method as earlier discussed by sanyal et al., 1971²². Briefly, the rats were fasted for 24 hrs before pylorus ligation but water was allowed ad libitum. At the end of 24 hrs starvation, rats were anaesthetized with pentobarbitone 35 mg/kg. Abdomen was opened by a midline incision and ligature was placed at the pyrolic and of the stomach taking care not to exclude a blood vessel. The abdomen was closed in two layers and rat was left in a cage with a false bottom of wide mesh wire gauge to prevent coprophagy. Water was withheld from 1 hr before pylorus ligation and till the end of 4 hr period when the rats were sacrificed by overdosing with ether. Immediately abdomen was again opened, cardiac and 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 number of ulcers was counted using a magnifying glass.

Mean ulcer score for each animal was expressed as ulcer index. The ulcers were graded using the following scoring system- 0= Normal mucosa; 0.5= Red coloration; 1.0=Spot ulcer; 1.5=Hemorrhagic streaks; 2.0=Ulcer 3 mm but d"5 mm; 3.0=Ulcer e" 5 mm.²³

Aspirin Induced Ulcers

The animals were treated with respective dose of 8 days as mentioned in previous model. After 8 days of treatment animals were fasted for 24 h. Ulcer was induced by administration of aqueous suspension of aspirin (200 mg/kg) 4 h later. The animals were sacrificed and stomach was opened to calculate the ulcer index as given earlier.²⁴

Statistical Analysis

All results were expressed as mean ±SEM for 6 rats. The difference among means been analysed by unpaired student's t-test (Newman-keuls multiple comparison test).

RESULTS AND DISCUSSION

We evaluated effects ethanol extract obtained from leaves *Ficus religiosa* in animals using the different standard experimental models of induced gastric ulcers. In case of Pylorus ligation model, the total acid output of the gastric juice and accumulation of gastric secretory volume were increased. Ethanolic extract with concentration of 250 mg/kg and 500 mg/kg resulted in a reduction in ulcer index in dose dependent manner with compared to control in Pylorus induced and Aspirin induced ulcers (Table 1 & 3, figures 1 & 2). Volume of gastric juice, free acidity and total acidity in case of pylorus ligation ulcers also results in the reduction manner (Table 2). Statistical analysis revealed that ethanolic extract of leaves of *F. religiosa* contains anti-ulcer activity due to the presence of flavonoids and sterol viz. stigmasterol Peptic ulcer in that part of the gastrointestinal tract (g.i.t) which is exposed to gastric acid and pepsin, i.e., the stomach and duodenum. The etiology of peptic ulcer is not clearly known.²⁵ Various mechanisms have been suggested for explaining the pathogenesis of peptic ulcer, which results due to an imbalance between the protective mechanisms and aggressive factors such as pepsin and acid.²⁶ A variety of psychometric, humoral and vascular derangements have been implicated and the importance of Helicobacter pylori infection as a contributor to ulcer formation and recurrence has been recognized.²⁵

Table 1: Effect of different leaf extract of *F. religiosa* on ulcer index in pylorus ligation induced ulcer

Group	Treatment	Dose (mg/kg)	Ulcer index (mm ² /rat)	% Protection
I.	Control	Pylorus ligation	10.29±0.02	-
II.	Ranitidine	50	3.7±0.05***	64.04
III.	Ethanolic extract	250	5.9±0.07***	42.66
IV.	Ethanolic extract	500	4.03±0.07***	60.08

Values are mean ± SEM (n=6) one way ANOVA followed by Student- Newman-keuls test.

*** represents most significant at p<0.001. when compared to control group.



Table 2: Effect of different leaf extract of *F. religiosa* on volume of gastric juice, Total acidity and Free acidity in pylorus ligation induced ulcer

Group	Treatment	Dose (mg/kg)	Volume of Gastric Juice (ml)	Free acidity (m/Eg/1)100g	Total acidity (m/Eg/1)100g
I.	Control	Pylorus ligation	3.3±0.17	31.9±0.50	90.4±0.54
II.	Ranitidine	50	1.5±0.14**	6±0.177***	9.7±0.15***
III.	Ethanolic extract	250	1.9±0.17***	10.4±0.09***	21.7±0.24***
IV.	Ethanolic extract	500	1.5±0.28***	2.1±0.18***	15.1±0.27***

Values are mean ± SEM (n=6) one way ANOVA followed by Student- Newman-keuls test

** represents more significant at p<0.001. when compared to control group.

*** represents most significant at p<0.001. when compared to control group.

Table 3: Effect of different leaf extract of *F. religiosa* on ulcer index on Aspirin induced gastric ulcers

Group	Treatment	Dose (mg/kg)	Ulcer index (mm ² /rat)	% Protection
I.	Aspirin	200	12.33±0.06	-
II.	Sucralfate	250	3.78±0.06***	69.34
III.	Ethanolic extract	250	5.1±0.0071***	58.63
IV.	Ethanolic extract	500	3.5±0.007***	71.61

Values are mean ± SEM (n=6) one way ANOVA followed by Student- Newman-keuls test

*** represents most significant at p<0.001. when compared to control group.

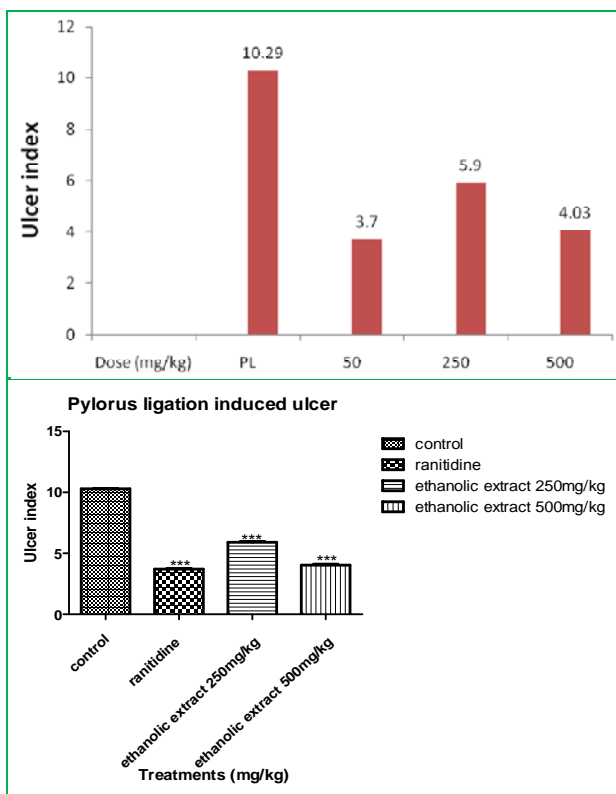


Figure 1: Effect of different leaf extract of *F. religiosa* on ulcer index in pylorus ligation induced ulcer

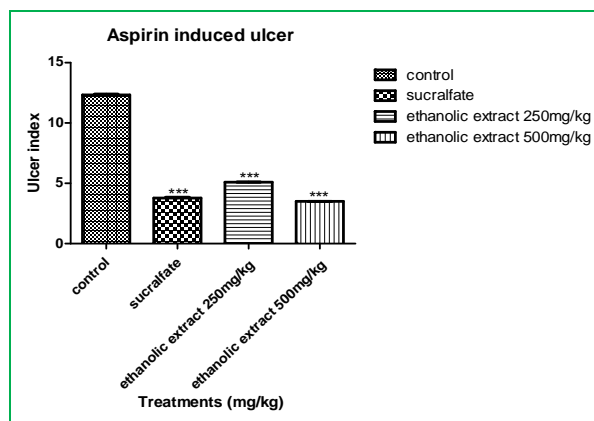
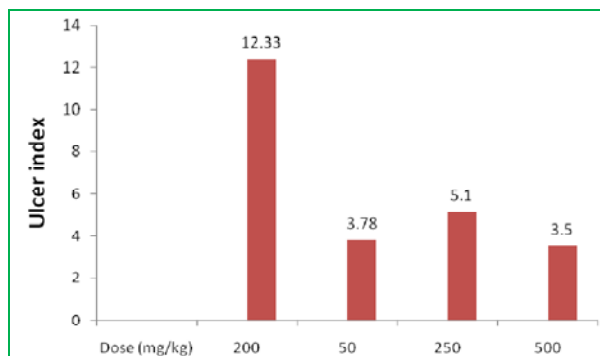


Figure 2: Effect of different leaf extract of *F. religiosa* on ulcer index on Aspirin induced gastric ulcers

CONCLUSION

Here present study was carried out to investigate anti-ulcer activity of ethanolic extract of *F. religiosa* leaves in pylorus ligated and aspirin induced ulceration in the Swiss albino rats. Pylorus ligation induced ulcer is one of the most widely used methods for studying the effect of drug on gastric secretion. The ligation of the pyloric end of the stomach causes accumulation of gastric acid causes ulcers in the stomach. Ethanol induced gastric ulcer was employed to study the cytoprotective effect of the extracts. Ethanol induced gastric lesion formation may be due to stasis in gastric blood flow which contributes to the development of the hemorrhage and necrotic aspects of tissue injury. The massive intracellular accumulation of calcium represents a major step in the pathogenesis of gastric mucosal injury. This leads to cell death and exfoliation in the surface epithelium. These factors are associated with the development of upper gastrointestinal damage including lesions, ulcers and life threatening perforation and hemorrhage. Approaches for the treatment of peptic ulcer are mainly H₂ antihistamines, proton pump inhibitors, anticholinergic.



The total acidity, free acidity, ulcer index of gastric secretions were increases. Standard dose of ranitidine and leaves extract of *F. religiosa* significantly decreased the gastric volume, total acidity, free acidity, and ulcer index. Similar studies support our results regarding the anti-ulcer effects.

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About Corresponding Author: Mr. Hemant Kumar



Mr. Hemant Kumar Graduate from U.P. Technical University and Post graduation also from U.P. Technical University and the project done from National Botanical Research Institute, Lucknow. At post graduation level taken specialization in Pharmacology, Pharmacognosy and completed master thesis in "To Investigate Pharmacognostic and Anti-ulcer Activity of *Ficus religiosa* L. on experimental Animals" and also guiding the post graduate students.