Assessment of Antiulcer Activity of Ethanol Extract of *Ficus religiosa* Fruit in Pylorus Ligated and Aspirin induced Ulceration in Experimental Animals

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Abstract

Ficus religiosa is a medicinal plant and scientifically documented for the pharmacological activities like antidiabetic, anti-inflammatory, antipyretic, etc. The present study was planned to investigate the antiulcer activity of ethanol extract of *Ficus religiosa* fruit in pylorus ligated and aspirin induced ulceration in experimental animals. The ethanol extract of fruits of *Ficus religiosa* were prepared by maceration. The antiulcer activity of ethanol extract were evaluated by using pylorus ligated and aspirin induced ulceration models. The administration of ethanol extract of *Ficus religiosa* at the dose of 200 mg/kg and 400 mg/kg significantly decreased the ulcer index, pH, gastric volume, free acidity and total acidity compared to control group. The findings proposed the antiulcer activity of ethanol extract of *Ficus religiosa* fruit.

1 Introduction

Peptic ulcers are a broad term that includes ulcers of digestive tract in the stomach or the duodenum. It is characterized by the disruption of the mucosal integrity of the esophagus, stomach, or duodenum¹. The various reports indicates that old age group patients are more susceptible to gastric ulcer. Younger individuals have higher risk of duodenal ulcers². Acute peptic ulcers involve tissues down to the depth of the submucosa. The lesions may be single or multiple, and it develop due to severe illness, shock, burns, severe emotional disturbance, and postsurgical complications. Chronic peptic ulcers penetrate through the epithelial and muscle layers of the stomach wall.

There are several symptoms of ulcer like changes in appetite, nausea, bloody or dark stools, weight loss, indigestion, vomiting and chest pain. Complications of peptic ulcers include haemorrhage, perforation, pyloric stenosis and the development of malignant tumors. Poor digestion and elimination, improper metabolism, mental and physical stress, and difficult to digest food enhance the development of ulcers. Peptic ulcer can be categorized on the basis of location (gastric

ulcers are located in the lining of the stomach, duodenal ulcers are located in the duodenum) and on the severity of disease. Numerous other factors are also responsible for progression of peptic ulcers like Tumor Necrosis Factor- α (TNF α), Reactive Oxygen Species (ROS), release of histamine, incidence of apoptosis and bile acids secretion³.

Ulcers are primarily caused by an imbalance between some endogenous aggressive and protective factors in the stomach such as acid-pepsin secretion, integrity of the mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins, and growth factors⁴. Several factors are also associated in the occurrence of peptic ulcer including stressful lifestyle, alcohol consumption, use of steroidal and non-steroidal anti-inflammatory drugs (NSAIDs; example, aspirin), *Helicobacter pylori* infections, smoking, lower socio-economic status and family history⁵. Although ulcer is not a deadly disease, it can lead to more serious complications like gastrointestinal bleeding, perforations, penetration of ulcer into adjacent organs and gastric outlet obstruction⁶.

Medications are used to relieve the pain, heal ulcerations and delay recurrence of ulcerations. These include antibiotics, antacids and proton pump inhibitors⁷. Several drugs are available in the market for gastric ulcer therapy; however, most of these drugs are associated with unwanted side effects⁸. The 75-80% of the world population still used herbal medicine mainly in developing countries, for primary health care because of better compatibility with the human body, and lesser side effects. Preliminary photochemical screening of this medicinal plant identified in the presence of important secondary metabolites like flavonoids and tannins which are the active principle of anti ulcer activity. Meteria medica provides lots of information about ethno medicinal herbs, which are valuable as antiulcer agents. Various plants like *Excoecaria agallocha*, *Mentha arvensis*, *Utleria salicifolia*, *Embllica officinalis*, *Ficus arnottiana*, *Alstonia Scholaris*, *Asparagus racemosus Willd*, *Azadirachta indica*, *Bauhinia variegata*, *Butea frondosa*, *Carica papaya*, *Annona squamoza* etc. proved active in antiulcer therapy. The use of traditional and modern knowledge can produced better antiulcer drugs with fewer side effects.

Ficus religiosa is an important traditional medicinal plant, belongs to family Moraceae. All the parts of the plants have medicinal properties. *Ficus religiosa* is affirmed the phytoconstituents of tannins, phenols, flavonoids, alkaloids and steroids, vitamin K, n-octacosanol, methyl oleanolate, lanosterol, β -sitosteryl-Dglucoside, stigmasterol, lupen-3-one, amino acids, phenylalanine and isoleucine, carbohydrate, lipid and minerals such as calcium, sodium, potassium, and phosphorus^{9,10}. Bark of the plant is used as gonorrhoea, diarrhea, dysentery, cervical cancer, epilepsy, leucorrhoea, menorrhagia, vaginal and other urogenital disorders haemorrhoids, ulcers, skin diseases and gastrophelcosis. It is also useful in inflammation, anti-anxiety, burning sensation, anti-bacterial, analgesic, anti-diabetic and anti-oxidant¹¹⁻¹³. Hence it was planned to evaluate the antiulcer activity of ethanol extract of *Ficus religiosa* fruit in pylorus ligated and aspirin induced ulceration in experimental animals.

2 Materials and Methods

2.1 Collection and authentication of plant material

The fruits of *Ficus religiosa* was collected from R. K. Pharmacy College, Kashipur, Surai Sathiaon, Azamgarh, Uttar Pradesh. The plant was authenticated by Prof. Nawal Kishore Dubey, Department of Botany, Banaras Hindu University Varanasi, India, and voncher specimen no-Morace 2018/1 was deposited in the herbarium of BHU Varanasi for future reference.

2.2 Preparation of extract

The dried fruits powdered were macerated with ethanol for 7 days. The menstrum was filtered and again macerated the exhausted powder with ethanol for four days and again repeated for third times. The menstrum obtained from 1, 2 and 3 extraction were combined and concentrated using rotary evaporator at 50

°C. The dried ethanol extract was kept in refrigerator for further use.

2.3 Pylorus ligation induced ulcer

The swiss albino rats were divided into different groups and each group have six animals:

Group I received normal saline

Group II received only aspirin (200 mg/kg)

Group III received ethanol extract (200 mg/kg)

Group IV received ethanol extract (400 mg/kg)

Group V received ranitidine (50 mg/kg)

The animals of groups III to V received aspirin at a dose of 200 mg/kg after 2 hr pretreatment of the extract and standard drug. The animals were anaesthetized with pentobarbitone 35 mg/kg on 8 day after fasting of 18 hr. 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 vessels. At the end of 4 h after ligation, the rats were sacrificed with excess of anaesthetic ether and the stomach was dissected out. The ulcer index, %protection, volume of gastric juice, free acidity, and total acidity were determined.

2.4 Aspirin induced ulcers

The swiss albino rats were divided into different groups and each group have six animals:

Group I received normal saline and served as normal group

Group II received aspirin 200 mg/kg on the 7 day of experiment

Group III received ethanol extract (200 mg/kg) for 7 days

Group IV received ethanol extract (400 mg/kg) for 7 days

Group V received ranitidine (50 mg/kg)

On 7th day, Aspirin (200 mg/kg) was administered to the all animals other than normal group with prior fasting of 24 h. The animals were sacrificed 4 h after administration of aspirin and the stomach part was excised, cut along the greater curvature, washed carefully with 5.0 mL of 90% NaCl and ulcer areas on the stomach's surface were examined macroscopically and measured on millimetre-square paper. The sum of area (mm²) was expressed as UI and percentage inhibition was calculated¹⁴⁻¹⁶.

2.5 Statistical analysis

The data are expressed as mean $\pm$ standard error mean and statistical comparisons were analysed using the statistical package for social science employing one-way analysis of variance followed by Dunnett's test. The results were considered statistically significant if the P values were less than 0.05.

3 Results and Discussions

Antiulcer activity of ethanol extract of fruit of *Ficus religiosa* was evaluated in pylorus ligated and aspirin induced ulceration in experimental animals. In pylorus ligated animals the gastric acid discharge is a significant factor for production of ulceration. At the point when aspirin was directed to pylorus ligated rats it further bothered the acid and the obstruction of the gastric mucosa was diminished consequently forcing wide damage to the glandular area of the stomach. In pylorus ligation model, the animal treated with aspirin significantly increased the ulcer index, pH, gastric volume, free acidity and total acidity compared to normal group. The administration of ethanol extract of *Ficus religiosa* at the dose of 200 mg/kg and 400 mg/kg significantly decreased the ulcer index, pH, gastric volume, free acidity and total acidity compared to control group (Table 1). The ranitidine treated

animals also significantly decreased the ulcer index, pH, gastric volume, free acidity and total acidity. The outcomes proposed the antiulcer activity of ethanol extract of *Ficus religiosa*.

The aspirin induced ulcer animal model shows that the administration of aspirin to the experimental animals of control group significantly increased the ulcer index, pH, gastric volume, free acidity and total acidity compared to normal group. This suggest the ulcer has been induced into the animals. The animals treated with the ethanol extract of *Ficus religiosa* at the dose of 200 mg/kg and 400 mg/kg significantly reduced the ulcer index, pH, gastric volume, free acidity and total acidity compared to control group (Table 2). The ranitidine treated animals also significantly decreased the ulcer index, pH, gastric volume, free acidity and total acidity. The findings outcomes offered the antiulcer activity of ethanol extract of *Ficus religiosa*.

Table 1: Effect of ethanol extract of *Ficus religiosa* pretreatment on pylorus ligation-induced gastric ulcer

Group	Treatment	Ulcer index	pH	Gastric volume	Free acidity	Total acidity
I	Normal saline	3.18±0.13	3.11±0.02	1.15±0.34	34.27±1.13	43.28±2.32
II	Aspirin (200 mg/kg)	9.45±0.32 ^a	1.26±0.05 ^a	3.29±0.76 ^a	78.69±2.05 ^a	86.52±1.57 ^a
III	Ethanol extract of <i>Ficus religiosa</i> (200 mg/kg)	5.92±0.11*	4.31±0.01*	1.24±0.15*	40.53±1.67*	48.12±1.34*
IV	Ethanol extract of <i>Ficus religiosa</i> (400 mg/kg)	3.46±0.07*	5.03±0.07*	0.67±0.54*	34.62±0.87*	40.45±2.13*
V	Ranitidine (50 mg/kg)	3.12±0.08*	5.27±0.04*	0.51±0.28*	29.71±1.43*	38.32±1.24*

Value are mean ±SEM, *p<0.05 represents significant difference from control group, while ^ap<0.05 represents significant difference from normal group

Table 2: Effect of ethanol extract of *Ficus religiosa* in aspirin induced gastric ulcers in rats

Group	Treatment	Ulcer index	pH	Gastric volume	Free acidity	Total acidity
I	Normal saline	3.47±0.49	3.31±0.07	1.42±0.51	30.73±0.76	38.14±0.17
II	Aspirin (200 mg/kg)	12.19±0.26 ^a	1.05±0.02 ^a	6.13±0.32 ^a	70.53±0.54 ^a	81.37±0.48 ^a
III	Ethanol extract of <i>Ficus religiosa</i> (200 mg/kg)	4.79±0.63*	3.49±0.06*	1.84±0.58*	37.58±0.16*	43.18±0.28*
IV	Ethanol extract of <i>Ficus religiosa</i> (400 mg/kg)	3.21±0.13*	4.75±0.03*	0.91±0.42*	29.17±0.83*	37.55±0.19*
V	Ranitidine (50 mg/kg)	3.04±0.42*	4.94±0.01*	0.46±0.29*	27.42±0.36*	35.24±0.23*

Value are mean ±SEM, *p<0.05 represents significant difference from control group, while ^ap<0.05 represents significant difference from normal group

Aspirin medicine origins a portion subordinate decrease in mucosal prostaglandin E₂ and prostaglandin I₂ biosynthesis joined by an expansion in the mean of gastric ulceration. It is along these lines sensible to expect that the perceived gastric mucosal injury instigated by aspirin is because of insufficiency of mucosal prostaglandin¹⁷. The present study examination uncovers that the ethanol extract of *Ficus religiosa* at the dose of

200 mg/kg and 400 mg/kg decreased the ulcer index and expanded the gastric pH of aspirin induced ulcer models.

4 Conclusion

The findings of present study suggested the ethanol extract of *Ficus religiosa* exhibited significant antiulcer activity. Further, cell line study is required for a clear understanding of the mechanism of action.

5 Conflict of interest

None

6 Author's contributions

HY, VKM, BY, RY, AKY, AR and RY equally contributed in the experimental work. The manuscript has been checked and approved by all authors before submission to the journal.

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