

ANTI-ULCER ACTIVITY OF ETHANOLIC EXTRACT OF STEM BARK OF *FICUS RELIGIOSA* IN WISTAR ALBINO MALE RATS: HISTOLOGICAL, BIOCHEMICAL AND SPERM ABNORMALITY PERTAINING TO THE DISEASE

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ABSTRACT

Ficus religiosa is being used in Ayurvedic medicine for the treatment of various diseases including gastric ulcer. The present study was undertaken to validate the anti-ulcer potential of the ethanolic extract of the stem bark of *F. religiosa* against aspirin – induced gastric ulcer. The plant extract (200 mg /kg) reduced the ulcer and also increased the pH of gastric acid while at the same time reduced the volume of gastric juice and total acidity. In conclusion, the present study provides preliminary data on the anti-ulcer potential of *F. religiosa* stem bark and supports the traditional use of the plant for the treatment of gastric ulcer.

KEYWORDS: Gastric ulcer, aspirin induced, *Ficus religiosa*, ayurvedic medicine, anti-ulcer potential.

INTRODUCTION

Peptic ulcer is the term designated for localized destruction of the inner wall or mucosa of the stomach (gastric ulcer) or the upper part of the small intestine (duodenal ulcer). Peptic ulcer generally occurs when there is an imbalance between aggressive gastric factors (acids, pepsin) and the maintenance of the mucosal integrity through endogenous defense mechanism. Peptic ulcer is the most common gastrointestinal disorder in clinical practice.

Non-steroidal anti-inflammatory drugs (NSAIDs) like aspirin causes gastric mucosal damage by decreasing prostaglandin levels through the inhibition of prostaglandin (PG) synthesis. The excess gastric acid formation by prostaglandins includes both increase in mucosal resistance as well as a decrease in aggressive factors, mainly acid and pepsin. Moynihan, an Irish surgeon was the first to relate the clinical symptoms of peptic ulcer disease with the pathological findings (Gibioki, 1987). It has been reported that small ulcers may not cause any symptoms and large ulcer can cause serious bleeding. The most common symptom is burning pain, especially just below the breast bone. Gastric ulcer pain may be less severe than duodenal ulcer pain and is noticeably higher in abdomen. Vomiting might be related to partial or complete gastric outlet obstruction. Epigastric tenderness, melena resulting from acute or sub-acute gastrointestinal bleeding and complete gastric outlet obstruction may also occur in ulcer disease (Le, 2009).

The success of commercially available anti-ulcer drugs such as proton pump inhibitors, H₂ receptors, cytoprotectants, demulcents, anti-cholinergics, antacids and prostaglandin analogues are used in the treatment of gastric ulcer is usually overshadowed by various side effects (Reilly, 1999). Herbal medicines are considered as better alternatives for the treatment of peptic ulcer (Vanisree *et al.*, 2002). The natural drugs were found to be the safer alternatives for the treatment of gastric ulcer (Revathi *et al.*, 2014). Herbal medicine is a 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 (Revathi *et al.*, 2017). This has led to the belief that natural products are safe because they are more harmonious with biological systems (Revathi *et al.*, 2015).

One of the plants that have been traditionally used in the Indian and Malays folklore medicine to treat gastric ulcer is *Ficus religiosa* L., which belongs to the family Moraceae. *F. religiosa* known in India as pimpal, peepal and pimpalla, is widely distributed in northern part of India. Different parts of this plant is used in traditional medicine for about 50 types of disorders including asthma, diabetes, epilepsy, gastric problems and inflammatory disorders, infectious and sexual disorders. Damanpreet and Rajesh (2009) proved that the methanolic extract of *F. religiosa* had anti-convulsant activity. Scientifically, the methanol bark extract of *F. religiosa*, which contained carbohydrates, flavonoids,

aminoacids, steroids, saponins and tannins (Uma *et al.*, 2009). In view of this, the present study evaluated the protective effects of standardized extract of *F. religiosa* stem bark against aspirin induced ulcer in albino rats. Despite claim of its potential in the treatment of gastric ulcer, this plant has been claimed to protect sperm abnormality too. Hence this study can be designed to find the potential of the stem bark extract in the treatment of ulcer and sperm disorders.

MATERIALS AND METHODS

The stem bark of *Ficus religiosa* was collected from Palakarai, Tiruchirappalli, Tamil Nadu, India. The preparation of stem bark extract was carried out according to the method of Oktay *et al.* (2003). Approximately 100gm of *F. religiosa* stem bark was extracted using 99% of pure ethanol in the ratio 1:2.

Male albino Wistar rats (*Rattus norvegicus*) weighed 120-130g body weight, were used as experimental animals for the present study. Animals were maintained in optimum conditions, provided with standard food and water *ad libitum*. Institutional animal ethical committee approvals were taken prior to perform this work.

Experimental design

The animals were divided into four groups and treated with the respective solutions as given below:

Group 1: control – vehicle (water 1ml)

Group 2: Negative control – aspirin (200mg/kg body weight)

Group 3: Ranitidine (200mg/kg body weight)

Group 4: *Ficus religiosa* stem bark extract (200mg/kg body weight)

The antiulcer activity of the stem bark extract of *F. religiosa* was evaluated by measuring the biochemical parameters such as alkaline phosphatase (Burtis *et al.*, 1998) and lactate dehydrogenase. And also the histological changes and sperm abnormalities were observed.

Sperm morphology assessment by WHO criteria

Following liquifaction, 10 μ L of semen was spread onto a glass slide and allowed to air-dry at room temperature. The smears were then stained with *Giemsa* stain and smear morphology was assessed according to WHO criteria. Smear using brightfield illumination at final magnification of 1000x and oil immersion.

Histology

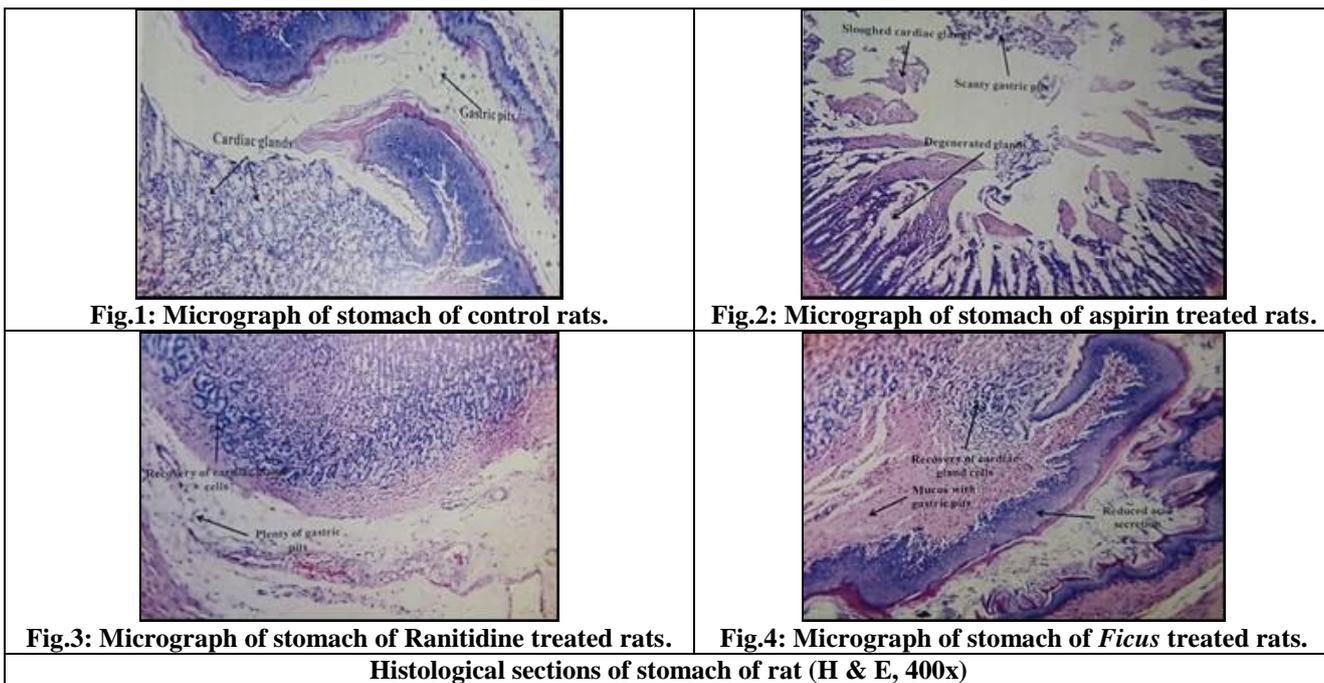
The histology of tissue was studied adopting the routine paraffin method and resin embedding method. A section of tissue must be mounted over the slide for microscopic studies.

RESULTS AND DISCUSSION

The stomach functions both as a reservoir and as a digestive organ. It empties its contents in small portion (suitable for continued digestion) into the small intestine.

Anatomically, the stomach is divided into a cardiac part, fundus, body or corpus and a pyloric part (pyloric antrum and pyloric canal). Histologically, most of the layers of the wall of the stomach appear similar in its different parts. Regional differences are mainly restricted to the appearance of the gastric mucosa (Fig. 1). The mucosa consist of epithelium, lamina propria, muscularis mucosae. The mucosa is thrown into longitudinal folds (gastric folds or rugae), which disappear when the stomach is fully distended. A network of shallow grooves divides the mucosa into gastric areas. The layers of the stomach were well arranged and visible as mucosal layer, submucosa layer and muscularis propria layer. The mucosa layer of the stomach of the control rats showed normal histology with intact epithelial lining and gastric pits. Almost the entire mucosa is occupied by simple, tubular gastric glands which open into the bottom of the gastric pits. The crypts were clearly demonstrated and well oriented.

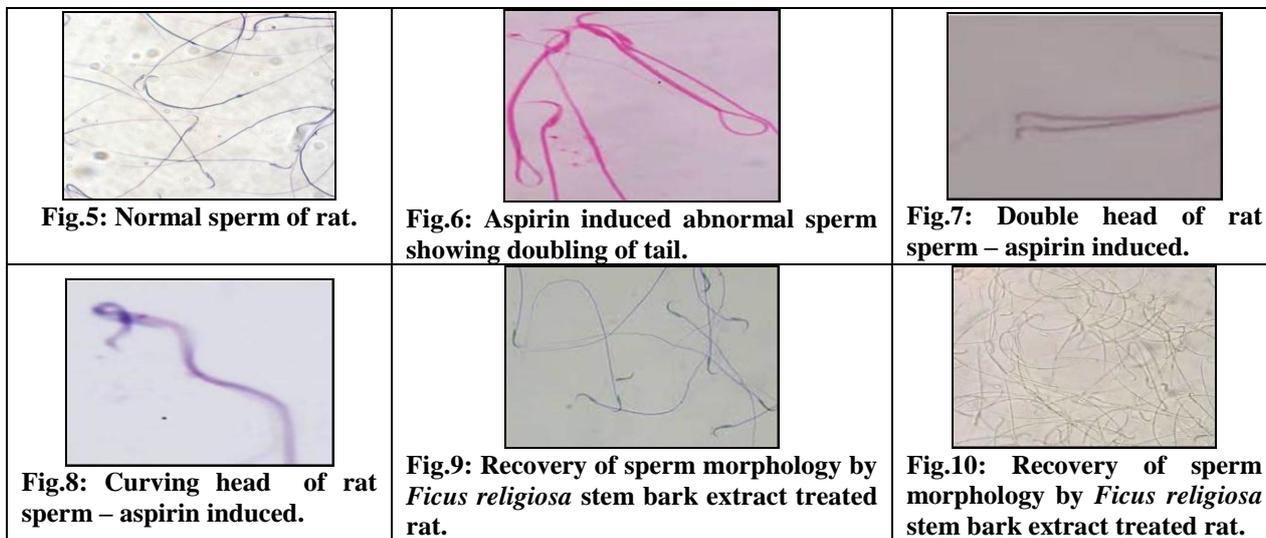
Sections stained with Hematoxylin and Eosin (H & E) displaying the regenerated lining epithelial width in stomachs of rats in extract treated (Fig. 4). The muscularis mucosae consist of a thin layer of smooth muscle at the boundary of the mucosa and submucosa. The aspirin treated groups showed moderate to heavy mucosa inflammation. The epithelial linings were seen to eroded and some of the crypts showed a lateral increase in size. There is no observed difference in the severity of histological alterations in aspirin treated groups (Fig. 2). Mucosal folds that decrease in size from the proximal to distal end are of different shapes in various segments (Fig. 2). Sometimes the mucosa is characterized by the presence of crypts associated predominantly with goblet cells intermixed with a few absorptive and entero-endocrine cells (Fig. 3). Paneth cells are scarce and are noted (Fig. 4). In the present study, *Ficus religiosa* alone or when administered along with ranitidine showed dose-dependent anti-ulcer effect in all the tested experimental models in rats. *Ficus religiosa* has been reported to reduce the development of induced gastric ulcers (Sonali *et al.*, 2013).



High levels are found in aspirin induced rat with 443 μ /L of LDH while in control it is only 278 μ /L. Plant extract treated rat showed almost near the value of control 287 μ /L, whereas the ALP result shows 85.4 μ /L in control and 36.6 μ /L in aspirin induced and 64.7 μ /L in *Ficus* treated rat.

Sperm morphology

The sperm head defects such as double head, curved head and double tail was markedly higher in the aspirin induced rats (Fig.5-8). The *Ficus* treated rat showed remarkable recovery both in head and tail (Fig.9 and 10).



IV. CONCLUSION

F. religiosa emerged as a good source of traditional medicine for the treatment of gastric ulcers. Although many of the experimental studies validated its traditional medicinal uses, but employed uncharacterized crude extract. Thus, it is difficult to reproduce the results and pinpoint the bio-active metabolite. Hence, there is a need of phytochemical standardization and bio-activity guided identification of bioactive metabolites. The results of few pharmacological studies and bioactive metabolites already reported in *F. religiosa* warrant detailed investigation to find the biochemical aspect such as LDH

and ALP levels. Sperm head and tail defect was found in aspirin induced. The outcome of these studies will further expand the existing therapeutic potential of *F. religiosa* and provide a convincing support to its future clinical use in modern medicine.

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