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# ANTIULCER ACTIVITY OF AQUEOUS EXTRACT OF LEAVES OF *SCOPARIA DULCIS* (Linn.) IN RATS

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## ABSTRACT

Anti-ulcer activity aqueous extract of leaves of *Scoparia dulcis Linn.*was investigated in pylorus ligation and ethanol induced ulcer models in experimental rats. In both models, the common parameter determined was ulcer index. Aqueous extract of *Scoparia dulcis* at doses of 250 and 500 mg/kg p.o produced significant inhibition of the gastric lesions induced by Pylorus ligation induced ulcer & Ethanol induced gastric ulcer .The extract (250 mg/kg & 500 mg/kg) showed significant ($P<0.05$) reduction in gastric volume, free acidity and ulcer index as compared to control. This present study indicates that aqueous extract of *Scoparia dulcis* have potential anti- ulcer activity in the both models. These results may further suggest that the extract was found to possess antiulcerogenic as well as ulcer healing properties, which might be due to its antisecretory activity.

## INTRODUCTION

Peptic ulcer disease is one of the most common gastrointestinal disorders, which causes a high rate of morbidity (Falk, 2001). Peptic ulcer is a conglomerate of heterogenous disorders which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and/or pepsin NSAID ingestion is associated with erosions, petechiae type C gastritis, ulceration interference with ulcer healing, ulcer complications and injury to the small and large intestine (Wallace, 1992).

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In recent years, a powerful association between peptic ulcers and infection of Helicobacter pylori has been adopted. At least 70-90% of patients with gastric ulcers and 80-95 % with duodenal ulcers are infected by H pylori and eradication of this microorganism seems to be curative for the disease (Mcquaid, 2002).

Although a number of antiulcer drugs such as H2 receptor antagonists, proton pump inhibitors and cytoprotectants are available for ulceration all these drugs have side effects and limitations (Ariyoshi *et al.*, 1986). Herbal medicine deals with plants and plant extracts in treating diseases. These medicines are considered safer because of the natural ingredients with no side effects (Clouatre and Rosenbaum, 1994). Screening plants for active drugs is still important and might provide a useful source of

new anti-ulcer compounds for developing pharmaceutical drugs or alternatively as simple dietary adjuncts to existing therapies (Borrelli**,** 2000).

*Scoparia dulcis* (Scrophulariaceae), commonly known as "sweet broom weed" is a perennial herb widely distributed in tropical and subtropical regions. It is widely used in Indian folk medicine for the treatment of stomach troubles, hypertension (Sadhu *et al.,* 2003), diabetes (Nath, 1943) bronchitis (Gonzales, 1986), and asanalgesic and antipyretic agents (Farias Freie et al., 1993). A number of different principles such as scoparic acid A, scoparicacid B, scopadulcic acid A and B, scopadulciol, and scopadulin have been shown to contribute to the observed medicinal effect of the plant (Hayashi et al., 1990). The present study was undertaken to evaluate anti-ulcerogenic properties of aqueous leaf extract of *Scoparia dulcis* in rats by using pylorus ligation ulcer model and ethanol induced ulcer model.

## MATERIALS AND METHODS

### Preparation of *Scoparia dulcis* leaf extracts

The fresh leaves of *Scoparia dulcis* was collected and is washed with tap water to removing adhering dust followed by distilled water, shade dried, and size reduced into small pieces. Five-hundred grams of fresh leaves of *Scoparia dulcis* were extracted with 1.5 ltr of water by the method of continuous hot extraction at 60°C for 6 h according to and the filtrate was concentrated at 40°C to constant weight in a rotavapor apparatus. The residue collected were thick paste, green in color and gumaceaous in nature and stored at -20°C, when needed the extract was dissolved in sterile water and used in the investigation (Jain, 1968).

### Animals

The study was conducted on male and female Wister rats (175 – 200 gm) housed in polypropylene cages under standard conditions of temperature (22 ± $2^0$C), relative humidity (60 ± 5%) and light (12h light/ dark cycle) were used. They were fed with standard pellet diet and water. The food was withdrawn 18 hours before the experiment but allowed free access of water. To avoid Coprophagy and fighting, the rats were fasted in wire-bottomed cages. All animal experiments were carried out in accordance with the guidelines of CPCSEA.

### Acute oral toxicity studies

A safe dose of the extract was determined by acute oral toxic class method of Organization of Economic Co-Operation and Development (OECD) as per 423 guidelines (Ecobichon, 1997). Rats were kept overnight fasting prior to drug administration. A total of five animals were used which received a single oral dose (2000 mg/kg) of *Scoparia dulcis* leaf extract. After the administration of extract, food was withheld for further 3 h. Animals were observed individually at least once during the first 30 min after dosing, periodically during the first 24 h (with special attention during the first 4 h) and daily thereafter for a period of 14 days. Once daily cage side observations included changes in skin and fur, eyes and mucous membrane (nasal) and also respiratory rate, circulatory (heart rate and blood pressure), autonomic (salivation, lacrimation, perspiration, piloerection, urinary incontinence, and defecation) and central nervous system (ptosis, drowsiness, gait, tremors and convulsion) changes. Mortality, if any, was determined over a period of 2 weeks (OECD, 2002).

### Pyloric ligation in rats

The animals were divided into 5 groups, each consisting of six rats. Control group were received distilled water orally. Second group of rats are pyloric ligated. Third and fourth Groups received aqueous leaf extract of *Scoparia dulcis* in a dose of 250 and 500 mg/kg. The fifth group of animals received Omeprazole in the dose of 20 mg/kg as a reference drug for ulcer protective studies. After 45 min of the treatment, pyloric ligation was done by ligating the pyloric end of stomach of rats of respective groups under ether anesthesia at a dose of 35 mg/kg of body weight. Ligation was done without causing any damage to the blood supply of the stomach. Animals were allowed to recover and stabilize in individual cages and were deprived of water during post-operative period. Rats were sacrificed after 4 h of surgery and ulcer scoring was done. Gastric juice was collected and gastric secretion studies were performed (Shay *et al.,* 1945).

**Ethanol induced ulcer model**

The ulcer was induced by administering ethanol. All the animals were fasted for 36 hours and then ethanol was administered to induce ulcer. The animals were divided into five groups, each consisting of six rats. The control Group received distilled water, second group received ethanol. Third and fourth groups received aqueous extract of *Scoparia dulcis* in a dose of 250 and 500 mg/kg. The fifth group of animals received Omeprazole in the dose of 20 mg/kg as a reference drug. The gastric ulcers were induced in rats by administrating absolute ethanol (90%) (1ml/200g.) Orally, after 45 min of aqueous extract of *Scoparia dulcis* and omeprazole treatment. They were kept in specially constructed cages to prevent coprophagia during and after the experiment. The animals were anaesthetized 1h latter with anaesthetic ether and stomach was incised along the greater curvature and ulceration will be scored. A score for the ulcer was study similar to pyloric ligation induced ulcer model (Mahmod, 2005).

**Scoring of ulcer** (Hikino *et al.,* 1985).

| | |
|---|---|
| Normal stomach | -0 |
| Red coloration | -0.5 |
| Spot ulcer | -1 |
| Hemorrhagic streak | -1.5 |
| Ulcers (< 2mm) | -2 |
| Ulcers (>2<4) Perforation | -3 |
| Ulcers (>4mm) | -4 |

Mean ulcer score for each animal will be expressed as ulcer index. The percentage of ulcer protection was determined by

$$\% \text{ of ulcer protection} = \frac{\text{Control mean ulcer index - Test mean ulcer index}}{\text{Control mean ulcer index}} \times 100$$

**Determination of free acidity**

$$\text{Acidity} = \frac{\text{Volume of sodium hydroxide} \times \text{Normality} \times 100\text{mEq/L/100g}}{0.1}$$

**Statistical analysis**

The values are represented as mean ± S.E.M, and statistical significance between treated and control groups was analyzed using of One way ANOVA, followed by Dennett's test where $P<0.05$ was considered statistically significant.

**RESULTS**

**Pyloric ligation induced gastric ulcer**

In pyloric ligation induced ulcer model, Oral administration of aqueous extract of *Scoparia dulcis* in two different doses showed significant reduction in ulcer index, gastric volume, free acidity, total acidity as compared to the control group. It was showing protection index of 69.7 % and 82.2 % at the dose of 250 and 500 mg/kg respectively in comparison to control whereas Omeprazole as reference standard drug was showing protection index of 86.2 %(Table-1).

**Ethanol-induced gastric ulcer**

In control animal, oral administration of absolute ethanol produced characteristic lesions in the glandular portion of rat stomach which appeared as elongated bands of thick, black & dark red lesions. extract of *Scoparia dulcis* has shown significant protection index of 68.7 % and 72.2 % with the dose of 250 and 500 mg/kg respectively in comparison to control, Omeprazole as reference standard drug was showing protection index of 80.6 %(Table-2).

**DISCUSSION**

The etiology of peptic ulcer is unknown in most of the cases, it is generally accepted that gastric ulcer results from an imbalance between aggressive factors and the maintenance of the mucosal integrity through the maintenance of the mucosal integrity through the endogenous defense mechanism (Szabo and Szlenji, 1987). Different therapeutic agents are used to inhibit the gastric acid secretion or to boost the mucosal defence mechanisms by increasing mucosal production, stabilising the surface epithelial cells or interfering with the prostaglandin synthesis (Tan et al., 2000). The prostaglandins can provide gastric cytoprotection in rats against strong necrotizing irritants without reducing gastric acid secretion (Yamamoto et al., 1992). The causes of gastric ulcer by pyloric ligation are believed to be due to stress induced increase in gastric hydrochloric acid secretion and/or stasis of acid.

**Table:-1** Effect of aqueous leaf extract of *Scoparia dulcis* on various parameters in pyloric ligation induced Gastric ulcers.

| Group | Treatment | Ulcer index | Free acidity meq/ltr | $P^H$ of gastric Juice | Gastric juice (ml) | Total acidity meq/ltr | Protection (%) |
|---|---|---|---|---|---|---|---|
| I | Normal (Distilled water) | ---- | 42.4±0.3 | 5.42±0.3 | 3.7±0.4 | 61.3±0.2 | ---- |
| II | Control (Pyloric ligation) | 15.2±1.2 | 96.7±1.2 | 2.61±0.2 | 9.2±0.2 | 113.6±0.2 | ---- |
| III | aqueous extract of *Scoparia dulcis* (250 mg/kg) | 4.6±0.5 | 44.7±0.3 | 4.97±0.2 | 5.4±1.2 | 76.3±0.4 | 69.7% |
| IV | aqueous extract of *Scoparia dulcis* (500mg/kg) | 2.7±0.4* | 40.8±0.2* | 5.61±0.4* | 4.2±0.4* | 62.7±0.6* | 82.2% |
| V | Omeprazole (20 mg/kg) | 2.1±0.5* | 39.4±0.2* | 5.72±0.2* | 3.9±0.2* | 60.1±1.4* | 86.2% |

**Table:-2** Effect of aqueous leaf extract of *Scoparia dulcis* on various parameters in ethanol induced Gastric ulcers.

| Group | Treatment | Ulcer index | $P^H$ of gastric juice | Protection (%) |
|---|---|---|---|---|
| I | Normal (Distilled water) | ---- | 5.37±0.3 | ---- |
| II | Control (Pyloric ligation) | 13.4±0.2 | 2.93±0.9 | ---- |
| III | aqueous extract of *Scoparia dulcis* (250 mg/kg) | 4.2±0.5 | 3.78±0.6 | 68.7% |
| IV | aqueous extract of *Scoparia dulcis* (500mg/kg) | 3.7±0.4* | 4.96±0.8* | 72.2% |
| V | Omeprazole (20 mg/kg) | 2.6±0.4* | 5.62±0.7* | 80.6% |

Values are express as mean ± SEM of observations, Statistical comparisons as follows: Significant *$p<0.05$ compared to control group.

The volume of secretion is also an important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid. The ligation of the pyloric end of the stomach causes accumulation of gastric acid in the stomach. This increase in the gastric acid secretion causes ulcers in the stomach. The lesions produced by this method are located in the lumen region of the stomach (Dhuley, 1999). Ethanol induced gastric lesion formation may be due to stasis in gastric blood flow which contributes to the development of the haemorrhage and necrotic aspects of tissue injury (Soll, 1990). Alcohol rapidly penetrates the gastric mucosa apparently causing cell and plasma membrane damage leading to increased intra cellular membrane permeability to sodium and water. 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 (Surendra, 1999). In the present study aqueous extract of *Scoparia dulcis* showed protection against gastric lesions in the experimental rats. Aqueous extract of *Scoparia dulcis* reduced the gastric volume, free acidity, total acidity and ulcer index thus showing the anti-secretory mechanism involved in the extract for their anti-ulcerogenic activity. Ulcer index parameter was used for the evaluation of anti-ulcer activity since ulcer formation is directly related to factors such as gastric volume, free and total acidity (Goel and Bhattacharya., 1991). The protection of aqueous leaf extract of *Scoparia dulcis* against characteristic lesions may be due to Scopadulcic acid B (SA-B), a novel diterpenoid, is the main ingredient of the biologically active compounds of Scoparia dulcis and its debenzoyl derivative, diacetyl scopadol (DAS), has been shown to inhibit gastric H+, K(+)-ATPase (Asano et al., 1990). Further studies

are needed for their exact mechanism of action on gastric acid secretion and gastric cytoprotection.

## REFERENCES


1. Ariyoshi L, 1986. Recurrence during maintenance therapy with histamine H2 receptor antagonist in cases of gastric ulcer. *Nithon Univ J Med* 28: 69-74.
2. Asano S, Reversible inhibitions of gastric H+, K(+)-ATPase by scopadulcic acid B and diacetyl scopadol. New biochemical tools of H+, K(+)-ATPase. J. Biol. Chem., 1990, 265, 22167–22173.
3. Borrelli F., Izzo AA., The Plant Kingdom as a Source of Anti-Ulcer Remedies. Phytotherapy Research. 2000; 14: 581-591.
4. Clouatre D Rosenbaum M 1994. *The Diet and Health benefits of HCA (hydroxycitric acid),* Keats publishing: New York, 31-32.
5. Dhuley JN. Protective effect of Rhinax, a herbal formation against physical and chemical factors induced gastric and duodenal ulcers in rats. *Indian J Pharmacol* 1999, 31, 128-32.
6. Ecobichon DJ., The basis of toxicity testing CRS Press, New York. 1997; 43-49.
7. Falk GW, Cecil Essentials of Medicine 5 th Edn., W.B.Saunders Company, Edinburgh. 2001: 334-343.
8. Farias Freie, Analgesic and anti-inflammatory properties of Scoparia dulcis L. extract and glutinol in rodents; Phytotherapy Research; 1993; 7; 408-414.
9. Goel RK, Gastro duodenal mucosal defense and mucosal protective agents. *Indian J Expl Biol* 1991; 29:701-14.
10. Gonzales Torres DM; Catalogo de Plantas Medicinales (y Alimenticias y Utiles) Usada en Paraguay; 1986; Asunción, Paraguay.
11. Hayashi T, Antiviral agents of plant origin III. Scopadulin, a novel tetracyclic diterpene from Scoparia dulcis L.; Chemical and Pharmaceutical Bulletin; 1990; 38; 945-947.
12. Hikino H, recent research on oriental medicinal plants, in economic and medicinal plant research, edited by H Wagner, H Hikino & N R Farnsworth (Academic press, London) 1985,53.
13. Jain SR: Hypoglycaemic principle in the Musa sapientum and its isolation. Planta Med 1968, 1:43-47.
14. Mahmod AA. *Int J Mol Adv Sci,* 2005, 1, 225.
15. Mcquaid KR., Current Medical Diagnosis and Treatment. 41 st Edn., Lange Medical Books/McGraw Hill Company, New York. 2002:616-621.
16. Nath MC; Investigations on the new antidiabetic principle (amellin) occurring in nature. Part I. Studies on some of its biochemical properties; Annals of Biochemistry and Experimental Medicine; 1943; 3; 55-62.
17. OECD, 2002. Acute oral toxicity. Acute oral toxic class method guideline 423 adopted 23.03.1996. In: Eleventh Addendum to the, OECD, guidelines for the testing of chemicals organization for economics co-operation, development, Paris, June, 2000.
18. Sadhu SK, Separation of Leucas aspera, a medicinal plant of Bangladesh, guided by Prostaglandin inhibitory and Antioxidant activities; Chem Pharm Bull; 2003; 51; 595-598.
19. Shay H, Simple method for uniform production of gastric ulceration in rat, *Gastroenterol*, 1945, 5, 43-61.
20. Soll AH. Pathogenesis of peptic ulcers and implication for therapy. *New Eng J Med* 1990, 322, 909- 16.
21. Surendra S. Evaluation of gastric antiulcer activity of fixed oil of tulsi and possible mechanism. *Indian J Exp Biol*, 1999, 36(3), 253-57.
22. Szabo, S., Szlenji, S. 1987. Cytoprotection in gastrointestinal pharmacology. *Trends Pharmacl. Sci*.8, 149-54.
23. Tan PV, Dimo T. and Dongo E (2000). Effects of methanol cyclohexane and methylene chloride extracts of Bidens pilosa on various gastric ulcer models in rats. *J. ethnopharmacol.* 73: 415-421.
24. Wallace JL. 1992. Non-steroidal anti-inflammatory drug gastropathy and cytoprotection–pathogenesis and mechanisms reexamined. *Scand J Gastroenterol* 27: S192, 3-8.
25. Yamamoto, K., (1992). Gastric cytoprotective antiulcerogenicactions of hydroxychalcones in rats. Planta Medica. 58: 389-393.