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Anti-Ulcer Activity of Methanolic Extracts of the Whole Plant of *Leptadenia pyrotechnica* Against Gastric Ulcer in Rats.

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ABSTRACT

The effect of methanolic extracts of the whole parts of *L. pyrotechnica* was investigated in rats to evaluate the anti-ulcer activity by using three models, i.e. Ranitidine and pyloric ligation models experimentally induced gastric ulcer. The parameters taken to assess anti-ulcer activity were volume of gastric secretion, PH, free acidity, total acidity and ulcer index. The results indicate that the alcoholic extract significantly ($P < 0.001$) decreases the volume of gastric acid secretion, PH and ulcer index with respect to control.

Keywords: *L. Pyrotechnica*, anti-ulcer activity, pyloric ligation, gastric ulcer.

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INTRODUCTION

Peptic ulcer disease is one of the most common gastrointestinal disorders, which causes a high rate of morbidity particularly in the population of non-industrialized countries. [1] Peptic ulcer occurs due to an imbalance between the aggressive (acid, pepsin and *Helicobacter pylori*) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, innate resistance of the mucosal cells) factors. [2] In Ayurveda, peptic ulcer mostly refers to *Amlapitta* or *Parinamasula*. *Amlapitta* is a disease of the gastrointestinal tract, especially of the stomach. *Amlapitta* literally means, pitta leading to sour taste. [3] Number of drugs including proton pump inhibitors, prostaglandins analogs, histamine receptor antagonists and cytoprotective agents are available for the treatment of peptic ulcer. But most of these drugs produce several adverse reactions including toxicities and even may alter biochemical mechanisms of the body upon chronic usage. [4] Hence, herbal medicines are generally used in such cases when drugs are to be used for chronic periods. Several natural drugs have been reported to possess anti-ulcerogenic activity by virtue of their predominant effect on mucosal defensive factors. [5-6]

Leptadenia pyrotechnica (Forssk.) Decne (Synonym-*L. Spartinum* Wight) locally known as Khimp or Khip (Rajasthan), Khimparlo, Thahawar, Ranser (Gujarat), Broom bush (English) is an erect, ascending, shrub up to 1.5m-3m high with green stem and pale green alternating bushy branches with watery sap. Leaf is rarely found and are deciduous when present are 2.5-6.5 x 0.2-0.3 cm, sessile, narrowly linear to linear lanceolate, caduceous. Flowers are in cluster lateral umbellate cymes, greenish yellow. Corolla –lobes valvate, outer corona is of 5 scales, stamina corona of raised undulate fleshy ring. Each flower is bisexual pentamerous actinomorphic, sepals joined at base only, corolla sympetalous. Follicles 7.0-14.0 x 0.5-0.8 cm, terete, lanceolate, tapering to slender beak, glabrous. Seeds are 5-7 mm long, ovate lanceolate, glabrous, comose (hairy) with tufted hairs 2.5-3.5 cm long. Flowering and fruiting occurs from August to January. It is common throughout the state of Rajasthan and found in dry habitats particularly in desert zones. In India it is commonly found in Banswara, Palod, Dungarpur and Kota [7]. Whole plant seeds and flowers are used for different purposes. Its fiber is used as antihistaminic and expectorant [8]. Fresh juice of the plant is used for abortion [9]. Plant sap is applied to eczema and other skin diseases and is also given in diabetes [10]. Whole plant is used in treating wounds in Yemen folk and proved to have antibacterial activity against *Staphylococcus aureus* & *Bacillus subtilis* [11,12]. The latex or the leaf paste is applied over the thorn injury for thorn removal [13]. Whole plant infusion is mixed with buttermilk and given for uterine prolapse and stomach disorders in Sariska region of Rajasthan [14]. It is used to cure constipation and is considered good for health in Bikaner region of Rajasthan [15]. In the Sudanese region of central Sahara it is traditionally used in fever, cough, kidney disorders, stones, urinary disease [16]. The present investigation was undertaken to evaluate anti-ulcer activity of methanolic extracts of the whole parts of *L. pyrotechnica*.

MATERIALS AND METHODS

Plant material

The plant of *Leptadenia pyrotechnica* was collected from “Kagore” village of Jaipur, Rajasthan, India in the month of January. It was authenticated by Dr. D. C. Saini, Sr. Scientist,

BirbalSahni Institute of Palaeobotany, Lucknow, Uttar Pradesh, India. [Voucher registration number 15531]

Preparation of extract

The successive extraction of powdered material was carried out in several batches using different solvents in increasing order of polarity in a soxhlet apparatus by hot percolation technique. The solvents used were petroleum ether, chloroform, acetone, methanol and distilled water. The powdered material of *Leptadenia pyrotechnica* was evenly packed in a soxhlet extractor for about 36 hours with different solvents. The temperature was maintained (25°C- 100°C) on an electric heating mantle with thermostat control. The extracts were then concentrated by evaporating the solvent under reduced pressure. Preliminary phytochemical studies were carried out on methanolic extract to assess the presence of various phytoconstituents [17-18] and Antiulcer activity.

Experimental animals

Wistar albino rats of either sex, weighing 150 to 200 gm, were housed in groups of four per cage under controlled light (12:12 light: dark cycle) and temperature (25 ± 2°C). Environmental and behavioral assessment was conducted during the light cycle. Food (Golden feed, New Delhi, India) and water *ad libitum* was provided. The animals were acclimatized to laboratory conditions for seven days before commencement of experiments. All the procedure described, were reviewed and approved by Institutional Animal Ethical Committee.

Toxicity studies

Acute toxicity study was performed for Methanolic extracts of *Leptadenia pyrotechnica* according to the acute toxic classic method as per OECD guidelines [19]. (Ecobichon, 1997). Female albino rats were used for acute toxicity study. The animals were kept fasting for overnight providing only water, after which the various extracts were administered orally at the dose of 150mg/kg and observed for 14 days. If mortality was observed in two animals out of three animals, then the dose administered was assigned as toxic dose. If the mortality was observed in one animal, then the same dose was repeated to confirm the toxic dose. If mortality was not observed, the procedure was repeated for further higher doses such 50,100,150,200, 400,500 & 2000mg/kg body weight. The animals were observed for toxic symptoms for 72 h.

Pylorus ligation (SHAY) Rats

PROCEDURE

The pylorus ligation was performed according to the **Shay et al.**,

Gastric ulcers were produced by pylorus ligation, the rats were fasted for 24 h before pylorus ligation but water was allowed *ad libitum*.

The animals were divided into five groups:

- Group I - served as control and received vehicle.
- Group II- served as standard and received Ranitidine at a dose of 50 mg/ kg.
- Group III- served as test and received plant methanolic extract at a dose of 150 mg/kg.

At the end of 24h starved, rats were anaesthetized with pentobarbital sodium (35 mg/kg sub cutaneous) abdomen was opened by a midline incision and a ligature was placed at the pyloric end of the stomach taking care not to excluded any blood vessels. The abdomen was then closed in two layer and rats were left in a cage with the false bottom of wide mesh wire gauzed to prevent coprophagy. Water was withheld from one hour before pylorus ligation & till the end of 4 h period. The abdomen was opened, cardiac end of the stomach was dissected out and the content was drained into the glass tube. The volume of the gastric juice was measured and its ph was detected.[20]

Macroscopic evaluation of stomach

The stomach was then cut open along the greater curvature and the mucosa was washed under slow running tap water to remove the gastric contents and blood clots and examined by a 10X magnifier lens to assess the formation of ulcer. The numbers of ulcers were counted.

Scoring of ulcer was made as follows:-

Normal colored stomach:	0
Red colored:	0.5
Spot ulcer:	1
Hemorrhagic streak:	1.5
Deep ulcer:	2
Perforation:	3

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

Ulcer index (U_i) was measured by using following formula:

$$U_i = U_N + U_S + U_P \times 10^{-1}$$

Where

U_i = ulcer index; U_N = average number of ulcers per animal; U_S = Average number of severity score; U_P = Percentage of animals with ulcer [20, 21].

Percentage inhibition of ulceration was calculated as below:

$$\% \text{ Inhibition of ulceration} = \frac{(\text{Ulcer index}_{\text{control}} - \text{Ulcer index}_{\text{test}})}{\text{Ulcer index}_{\text{control}}} \times 100$$

STATISTICAL ANALYSIS

The statistical significance was assessed using one-way analysis of variance (ANOVA) followed by Bonferrone Test. The values are expressed as mean ± SEM and P<0.05 was considered significant.

RESULT & DISCUSSION

The methanolic extracts of the whole parts of *L. pyrotechnica* was evaluated for antiulcer activity using the pylorus ligation model in rat at a dose of 150 mg/kg body weight where as Ranitidine at a dose of 50 mg/kg was used as a standard and the results were shown in Table no 1.0, Fig no.1.0

Table no 1: Effect of methanolic extract of *L. pyrotechnica* on pylorus ligation- induced ulceration in rats

Group	Dose (mg/kg)	Ulcer index	% protection	Volume of gastric juice (ml)	pH of gastric juice
Control	--	0.17 ± 0.005	--	5.52 ± 0.61	2.0
Ranitidine	50	0.05 ± 0.02**	70.59	1.29 ± 0.13	6
Methanolic extract of <i>L. pyrotechnica</i>	150	0.07 ± 0.005**	58.82	5.2 ± 0.1	6

Antiulcer activity of methanolic extract of *L. pyrotechnica* by pylorus ligation. All the values are shown as mean ± Sem n = 6, *p < 0.05, ** p < 0.01, * p < 0.001 vs control. # p < 0.05,## p < 0.01, ### p < 0.001 vs standard.**

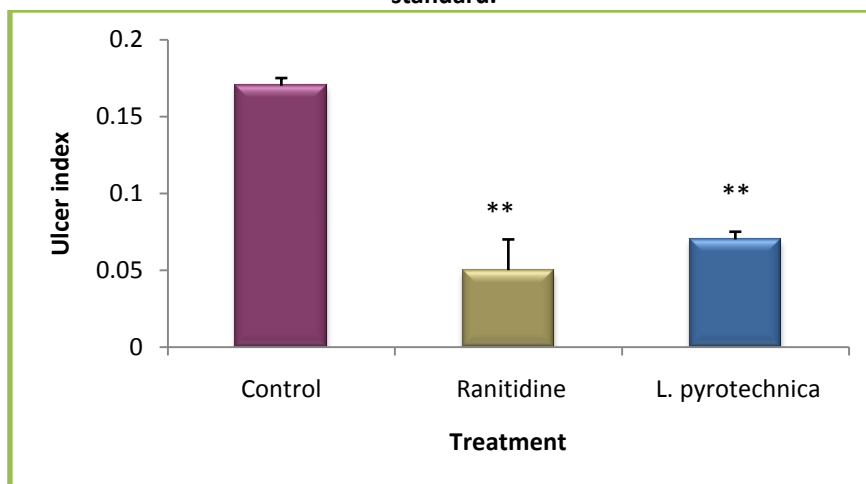


Fig no 1: Graph representing ulcer index in various groups.

The Ulcer index in pylorus ligation induced ulceration were found to be high in control and a significant difference in the mean ulcer index were observed in standard Rsnitidine (50 mg/kg) and in the methanolic extract of *L. pyrotechnica* 150 mg/kg dose.



Fig no 1.1: Image of rat's stomach after pylorus ligation. (A) Control group, (B) standard (ranitidine) group, (C) Test (*L. pyrotechnica*) treated group.

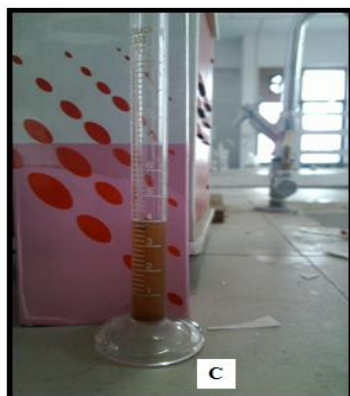
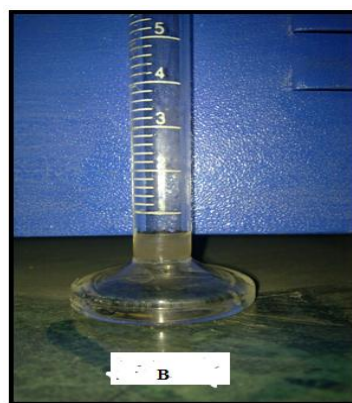


Fig no 1.2: Showing the volume of gastric juice in various treated groups. (A) Control group, (B) standard (ranitidine) group, (C) Test (*L. pyrotechnica*) treated group.

Dose of methanolic whole plant extract of *L. pyrotechnica* showed significant reduction in ulcer index but gastric volume was almost similar to the control also there is a increase in the pH of gastric juice as compared with control groups. It was showing protection index 58.85% at a dose of 150 mg/kg respectively as compared with standard drug ranitidine showed 70.59%. The cause of gastric ulcer pyloric ligation are believed to be due to stress induced increase in gastric hydrochloric acid secretion and volume of secretion is also important factor in the formation of ulcer due to exposure of the unprotected lumen of the stomach to the accumulating acid.

Pylorus ligation induced ulcers are due to auto digestion of the gastric mucosal barrier. These factors are associated with the development of upper gastrointestinal damage due to lesions, ulcers and life threatening perforation and hemorrhage. The significant antiulcer activity of *L. pyrotechnica* could be attributed to the flavonoid, alkaloids, tannins, glycoside and phenolic compound. Flavonoid are among the cytoprotective materials for which ulcerogenic efficacy has been extensively confined. It is suggested that these active compounds would be able to stimulate mucus, bicarbonate and prostaglandin secretion and counteract with deterioration effect of reactive oxidants in gastrointestinal lumen.[20,21,22] In conclusion, the methanolic extract of whole plants of *L. pyrotechnica* has a gastroprotective property against experimentally induced ulcer in rat and hence can be used to treat ulcer.

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