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Research Article

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EVALUATION OF ANTI-ULCER ACTIVITY OF *PAEDERIA FOETIDA* ROOT EXTRACTS IN EXPERIMENTALLY INDUCED GASTRIC ULCER IN RATS

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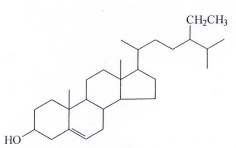
ABSTRACT
Paederia foetida Linn., a member of *Rubiaceae* is an extensive climber, known as Chinese flower in English, Gandhaprasarini in Hindi, Gandha bhadulia in Bengali, Prasarani in Sanskrit and Savirela in Telugu. It is found in the Himalayas from Dehradun eastwards up to an altitude of 1800m and also in Bihar, Orissa, Bengal, Assam and Araku vally in Visakhapatnam district of Andhra Pradesh. Since the plant was reported to have many medicinal uses, we taken up the plant to give scientific support to the folklore claim on the antiulcer activity of roots. The anti ulcer screening was performed using two methods that is pyloric ligation method and aspirin induced ulcerations in rats. Volume of gastric acid, total acidity and the free acidity were also measured to assess the anti ulcer potential. The present investigation therefore expressed that the roots of *P. foetida* exerts anti-ulcer activity which may be due to anticipated inhibition of H_2 receptors resulting in inhibition of gastric acid secretion elicited by histamine and gastrin. The work justifies its use in the traditional system of medicine.

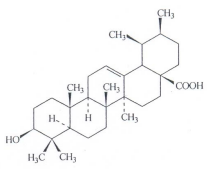
Key words: *Paederia foetida*, pyloric ligation method, Aspirin induced ulcers, Ranitidine, Sucralfate.

INTRODUCTION

Paederia foetida Linn, a member of *Rubiaceae* is an extensive climber; glabrous or puberulous. It is known as Chinese flower in English, Gandhaprasarini in Hindi, Prasarani in Sanskrit. It is found in the Himalayas from Dehradun eastwards up to an altitude of 1800 mt. Traditionally, the entire plant used for aphrodisiac, dysentery, stomach troubles, diuretic and liver complaints. The whole plant is regarded as a specific for arthritis and rheumatic affections, in which it is, administered both internally and externally[1]. The roots are used as emetic and the juice extracted from the roots is given in case of inflammation of the spleen and for pains in the chest and liver. The leaf juice is considered astringent and given to children for diarrhoea. A poultice of the leaves when applied to abdomen relieves distension due to flatulence; also used in herpes[2]. The boiled and mashed leaves are applied to the abdomen in cases of retention of urine, and the hot aqueous extract of the aerial parts are known to be used for treating liver diseases. The fruits are used to prevent toothache[3,4]. Presence of Iridoid monoterpenes, Fatty acids[5], Embelin and Friedelanol[6] was reported earlier. Other phytoconstituents reported include hentriacontane, hentriacontanol, ceryl alcohol, sitosterol, stigmasterol, campesterol, ursolic acid and epifriedelinol[7].



Stigmasterol



Ursolic acid

P. foetida was reported to possess anti diarrhoeal[8], hepatoprotective[9] and anti-inflammatory activity[10, 11], antioxidant and phenolic content[12]. Since the plant was reported to have many medicinal uses and being widely used in ethonobotonically for many ailments for human beings, the present study was designed to give scientific support to the folklore claim on the antiulcer activity of roots.

MATERIAL AND METHODS

Plant material

Fresh roots (1.5 kg) of *P. foetida* was collected from young matured plants from the Pakala region, Warangal district during early summer and authenticated by Prof. V. S. Raju, Taxonomist, Department of Botany, Kakatiya University, Warangal., A.P., India and a voucher specimen (KSR/11/2008) was deposited in the Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam, Andhra Pradesh, India. The material was dried and powered.

Preparation of the extract

The powdered plant material (380 g) of *P. foetida* was extracted separately with 2 liters of distilled water and ethanol by maceration process for 72 h. The solvents were then removed under reduced pressure and dried in desiccators [aqueous extract (designated as AEPF) yield 9.78%w/w and ethanolic extract (designated as EEPF) yield 2.97%w/w with respect to dry material]. The extracts were suspended in Tween 20 (20%v/v in distilled water) and used for the present study.

ACUTE ORAL TOXICITY STUDIES

Acute oral toxicity studies were performed according to OECD guideline No. 423. Three mice weighing between 25–30gm were used for study. The aqueous and ethanolic extracts of *P. foetida* were screened for the gross behavioral and toxicity studies in selected Swiss Albino Mice. Groups of mice comprising six animals each were treated with 100, 200, 400,800, 1000 and 2000 mg/kg of the extracts suspended in 0.5% w/v sodium carboxy methyl cellulose were administered orally, via a gastric catheter. The animals were then observed continuously for first four hours for any behavioral changes and for mortality if any at the end of 72 h. Both the aqueous and ethanolic extracts were found to be safe since no animal died even at the dose of 2000 mg/kg when administered orally, and the animals did not show any gross behavioral changes. Hence, aqueous and ethanolic extracts were selected for the present study.

PHARMACOLOGICAL STUDIES

Experimental animals for antiulcer activity

Adult Wistar albino rats of either sex weighing between 170-200 g were used for the study. The animals were housed in standard acrylic cages at room temperature for 48 h for acclimatization. They were fasted 24 h prior to commencement of the experimental procedure. The animals were deprived of food and water during the experimental period. The protocols were approved by Institutional animal ethical committee of Vaagdevi College of pharmacy,

Hanamkonda, Andhra Pradesh, India vide approval No. 1047/AC/09/CPCSEA.

Anti-ulcer activity of *P. foetida*

The antiulcer activity of the aqueous and ethanolic extract of *P. foetida* was evaluated on selected albino rats by both pyloric ligated ulceration model and aspirin induced ulceration model respectively.

Pyloric ligated ulceration

The selected animals were divided into four groups of six in each. Each group of the animals received one of the following test samples through oral route: 20%v/v tween 20 in distilled water (2 ml/kg), ranitidine (20 mg/kg), aqueous extract (200 mg/kg), ethanolic extract (200 mg/kg) respectively. After one hour, pylorus ligation was made under ether anesthesia. The animals were then returned to the observation chambers. After 4 h, the animals were sacrificed by decapitation, the abdomen of each animal was opened and the stomach was isolated after suturing the lower esophageal end. The gastric juice was collected by giving a small cut to the pyloric region just above the knot in a measuring cylinder and stomach was opened along the greater curvature. The mucosal layer was washed with 1 ml distilled water and the washings were added to the gastric secretions. The gastric contents were centrifuged at 2000 rpm for 10 min. The supernatant fluid (1 ml) was diluted with 9 ml of distilled water and then titrated against 0.01N sodium hydroxide solution using Topfer's reagent till the solution turns to orange colour. The volume of sodium hydroxide required corresponds to free acidity. The solution was further titrated till the solution regained pink colour. The volume of sodium hydroxide required corresponded to the total acidity[13, 14].

The internal lining of the stomach of each rat was then examined carefully for characterizing severity of ulcers. The ulcers were graded as follows,

0 = Normal coloured stomach, 0.5 = Red colouration,1 = Spot ulcers, 1.5 = Haemorrhagic streaks,2 = Ulcers ≥ 3 but ≤ 5, 3 = Ulcers > 5.

Aspirin induced ulceration

The selected animals were divided into four groups of six in each. Each group of animals received the test samples as earlier through oral route. Sucralfate (25 mg/kg) was used as reference standard. After 30 min, each animal was administered 200 mg/kg aspirin through oral route. After 1 h, pylorus ligation was made as per the procedure. The animals were sacrificed after 4 hr, the stomachs were opened along the greater curvature and carefully observed for severity of ulceration as described earlier[15, 16]. The results were depicted in Tab. No. 2.

Statistical analysis

The mean ulcer score of each animal was expressed as ulcer index. The results were expressed as mean ± S.E.M and tabulated in Table-1. Significance of differences between control and treated groups was determined using Student's *t*-test.

RESULTS AND DISCUSSION

The findings of the study revealed that the root extracts possess significant anti-ulcer activity. In pyloric ligated ulceration (*Shay* model), all the test samples were found to reduce the volume of gastric acid to a significant extent ($p< 0.01$), (Fig. No.1) where as ranitidine reduced the volume to the extent of $p<0.001$. The total acidity and the free acidity also registered significant decrease in a similar manner, (Fig. No. 2 & 3). The ulcer index was significantly reduced with all test samples (Fig. No.4, 5) the order of reduction of ulcer score observed was ranitidine < ethanol extract < aqueous extract.

In aspirin induced ulceration model, the extracts reduced the ulcer index significantly, but the stomach mucosal layer was found to be normal. (Fig 6, 7) The available literature information on possible mechanism of action of sucralfate reveals that it accelerates ulcer healing by forming ulcer adherent complex with proteinaceous exudates, as a result of which pepsin activity is inhibited, where as H_2 antagonists protect experimental animals from gastric ulceration induced by stress, pyloric ligation, aspirin, H_2 receptor agonists or cholinomimetics[16].

CONCLUSION

The present investigation therefore expressed that the roots of *P. foetida* exerts anti-ulcer activity which may be due to anticipated inhibition of H_2 receptors resulting in inhibition of gastric acid secretion elicited by histamine and gastrin. The work justifies its use in the traditional system of medicine.

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Table-1: Anti-ulcer activity of the aqueous and ethanolic extract of *P. foetida* on pyloric ligated rats.

Group	Treatment	Dose	Volume of gastric juice (ml.)	Total acidity (meq/lit)	Free acidity (meq/lit)	Ulcer index
I	Vehicle (20%v/v Tween 20)	2 ml/kg	4.21 + 0.16	16.43 + 0.33	3.05 + 0.09	3.82 + 0.21
II	Ranitidine	20 mg/kg	2.03 + 0.18**	6.52 + 0.22**	0.52 + 0.03**	0.68 + 0.11**
III	Aqueous extract of *P. foetida* (AQPF)	200 mg/kg	3.56 + 0.17*	12.26 + 0.29**	1.3 + 0.14**	1.85 + 0.26**
IV	Ethanolic extract of *P. foetida* (EEPF)	200 mg/kg	3.38 + 0.23*	10.08 + 0.49**	0.99 + 0.04**	1.37 + 0.28**

Results expressed as Mean + SEM from six observations

* $P < 0.01$, ** $P < 0.001$

Table No. 2 Anti-ulcer activity of the aqueous and ethanolic extract of *P. foetida* in Aspirin induced ulcers

Group	Treatment	Dose	Ulcer index
I	Vehicle (20%v/v Tween 20)	2 ml/kg	4.55+0.17
II	Sucralfate	25 mg/kg	0.38+0.25**
III	Aqueous extract of *P. foetida*	200 mg/kg	1.99+0.49*
IV	Ethanolic extract of *P. foetida*	200 mg/kg	1.67+0.20**

Results expressed as Mean + SEM from six observations
* P < 0.01, ** P < 0.001

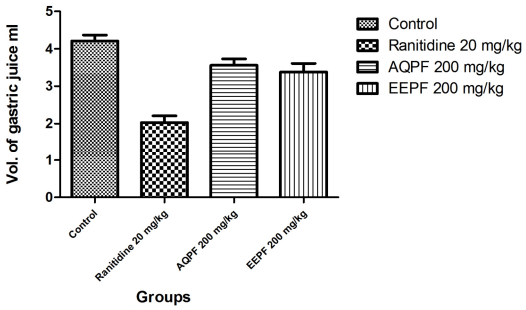

Fig. No. 1 Effect of *P. foetida on* Volume of gastric juice

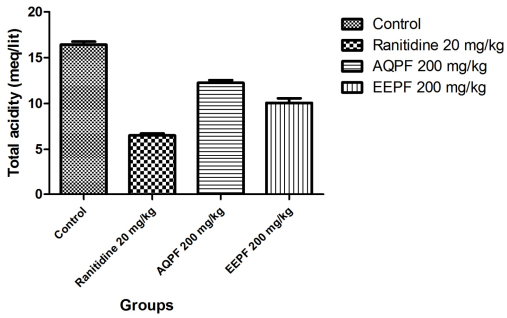

Fig. No. 2 Effect of *P. foetida on* Total acidity

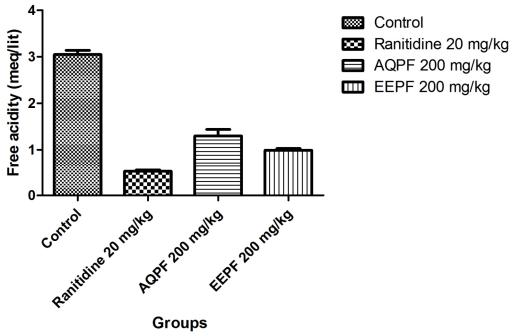

Fig. No. 3 Effect of *P. foetida on* free acidity

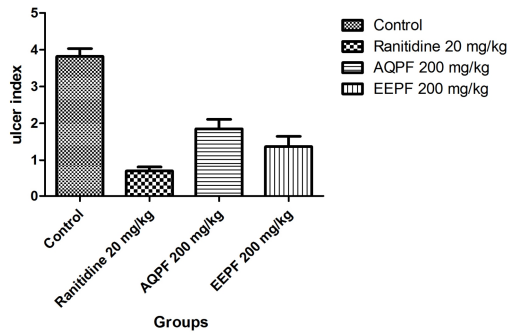

Fig. No. 4 Ulcer index of *P. foetida* in pyloric ligated rats

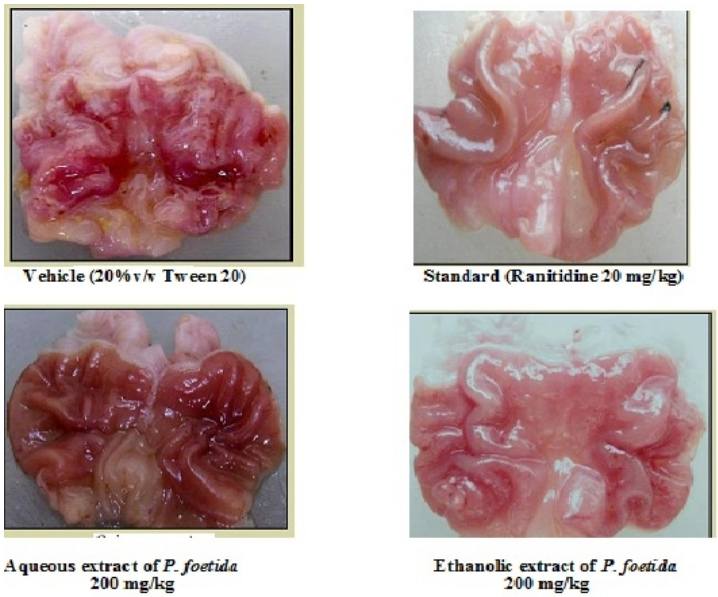

Fig. No. 5 Anti-ulcer activity of the aqueous and ethanolic extract of *P. foetida* on pyloric ligated rats

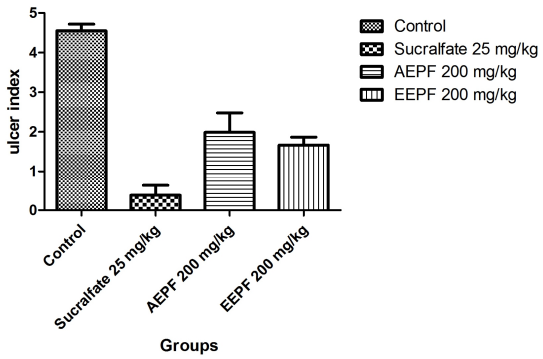

Fig. No. 6 Ulcer index of *P. foetida* in aspirin induced ulcers

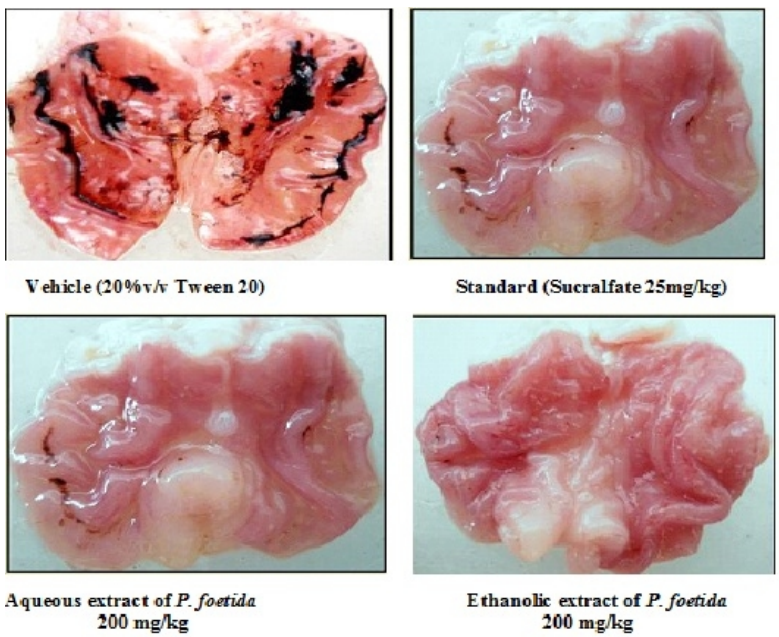

Fig. No. 7 Anti-ulcer activity of the aqueous and ethanolic extract of *P. foetida* in Aspirin induced ulcers

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