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Antiulcer Activity of Patol Churna against Experimental Gastro-duodenal Ulcers in Rats

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Abstract

Patol churna is a well known ayurvedic formulation of *Trichosanthes cucumerina* Linn. (cucurbitaceae) administered in case of number of alimentary and liver disorders. It is widely used in Indian folk medicine for variety of disease conditions. The aim of present study was to evaluate the antiulcer activity of 50% ethanolic extract of patol churna (PCE) using various experimental models of gastric and duodenal ulceration in rats. Oral administration of 50% ethanolic extract of patol churna was evaluated in rats against ethanol, aspirin and pylorus ligated gastric ulcers as well as cysteamine-induced duodenal ulcers. In all the models studied, the antiulcer activity of PCE compared with that of cimetidine (100mg/kg, p.o.), an H_2 receptor antagonist. PCE showed significant antiulcer activity in ethanol-induced and aspirin-induced gastric ulcer models. In 19 hrs pylorus ligated rats, significant reduction in ulcer index, total acidity and pepsin activity was observed with PCE, when compared with the control group. Mucosal defensive factors such as pH, mucin activity and gastric wall mucous content was found to be increased with PCE. PCE was also, afforded remarkable protection in cysteamine-induced duodenal lesions. The antiulcer activity of PCE was comparable with that of cimetidine. Thus, patol churna extract possess significant antiulcer activity against both gastric and duodenal ulcers in rats. The antiulcer activity may be attributed to its cytoprotective action and inhibition of acid secretary parameters.

Keywords: Antiulcer activity; Duodenal ulcer; Gastric ulcer; *Trichosanthes cucumerina* Linn; Patol churna

Introduction

Trichosanthes cucumerina Linn. (cucurbitaceae) is an annual climber and widely distributed throughout India, Ceylon, Malaya and North Australia. In Gujarat, the plant is known as 'Patola' or 'Kadvi Parval'. Patol churna is a well known ayurvedic formulation of *T. cucumerina* administered in case of number of alimentary and liver disorders. Whole plant is reputed for the treatment of hepatic and alimentary canal disorders. Fruits of *Trichosanthes cucumerina* are used as laxative, purgative, antipyretic, alexiteric and antiulcer agent. The leaves are good for bilious disorders [1]. Antidiabetic [2], hepatoprotective [3], anti-inflammatory [4], antifertility [5], antioxidant [6], antibacterial [7], antifungal [8] and antiviral [9] activities of the plant were reported. The fruits contain ascorbic acid, lycopene, phenols, flavonoids, alkaloids, tannins and saponins [6,10]. Present study was undertaken to evaluate the effect of 50% ethanolic extract of patol churna (PCE) in various experimental ulcer models.

Materials and Methods

Plant material and extraction

Patol churna, a readymade formulation powder was procured from the local market of Ahmedabad, India and authentication was done in the department of Pharmacognosy, L. M. College of Pharmacy, Ahmedabad. It was found to be a mixture of all the aerial parts of *Trichosanthes cucumerina*. The powder was extracted exhaustively with 50% ethanol by maceration at room temperature for 2 days with occasional shaking. The crude extract was dried at 40°C under vacuum (Yield – 11% w/w of dried powder). The pharmacological assays were arried out with aqueous solution of dried extract (PCE). The doses were expressed as mg of dried extract per kg of rat.

Drugs and chemicals

Cimetidine (Cadila, Ahmedabad) was used as reference standard. Aspirin (Cadila, Ahmedabad) and Cysteamine (Merck, Germany) were used for experimental induction of gastric and duodenal ulcers respectively.

Animals

Wister rats (200-250g) of either sex bred in Central Animal House facility of the institute were used. The animals were housed under standard conditions, maintained on a 12 hrs light/dark cycle and had free access to food and water up to the time of experimentation. The animals were acclimatized to the laboratory environment 1 hr before the experiments. Animals were randomly distributed into groups of 10 animals each. All experiments were conducted during the light period (08.00-16.00 hrs). All the protocols were approved by the Institutional Animal Ethical Committee (IAEC) and conducted according to the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiment on Animals).

Treatment

Freshly prepared aqueous solution of dried extract of patol churna (PCE) in suitable dilution was administered orally in the test animals. For the ethanol induced ulcer model, animals were divided in to five groups, each group consisting of six animals. Group 1 served as control group received distilled water (vehicle) 1 ml/kg, p.o., group 2-4 served as test groups received PCE (300, 500 and 800mg/kg, p.o.) and group

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5 served as positive. In all other models animals were divided in to 3 groups (n = 6) viz. control, test and reference standard. Test group received PCE at the dose of 500mg/kg, p.o. in aspirin induced, pylorus ligated and cysteamine induced ulcer model. Cimetidine (100mg/kg, p.o.) was used as reference standard in all experimental models.

Ethanol- induced gastric ulcer model: 1ml of 80% ethanol was administered orally to 36 hrs fasted rats [11]. PCE at the dose of 300, 500 and 800mg/kg was administered orally 1 hr before ethanol treatment. After 2 hrs of ethanol administration, animals were sacrificed and ulcer index of glandular mucosa was determined [12].

Aspirin-induced gastric ulcer model: Aspirin was suspended in 1% CMC in water and administered orally at the dose of 500mg/kg to 36 h fasted rats [13]. PCE (500mg/kg) was administered orally, 1hr before aspirin treatment. The rats were sacrificed 6 h after aspirin administration, the stomachs removed and opened along the greater curvature to determine ulcer index of glandular mucosa [12].

Pylorus ligation-induced gastric ulcer model: In 36 hrs fasted rats pylorus ligation were performed under light ether anaesthesia, care being taken not to cause bleeding or to occlude blood vessels. PCE at the dose of 500 mg/kg was administered orally immediately after pylorus ligation. 19 hrs after ligation, the rats were sacrificed. The stomachs were removed and opened along the greater curvature. The glandular portion of stomach was observed for measurement of ulcer index [14]. The contents were drained into tubes, centrifuged and subjected to analysis for various biochemical parameters. The volume and pH of gastric juice were measured. Total acidity [15], Total acid output [16], Pepsin activity [17], total carbohydrate [18] and protein content [19] were estimated. Finally, the total carbohydrate to protein (TC/PR) ratio i.e, mucin activity was derived. Gastric wall mucus content (GWMC) was measured from glandular portion of stomach [20] and was expressed as mg of alcian blue per g of wet glandular tissue [21].

Cysteamine-induced duodenal ulcer model: Cysteamine hydrochloride was administered in two doses of 400 mg/kg in 10% aqueous solution at an interval of 4 hrs to rats [22]. PCE was administered in a single dose (500 mg/kg, p.o.) 1 hr before the first dose of cysteamine. Parameters studied in this model were percentage mortality, total lesion area, score of intensity and ulcer index. Ulcer index was calculated as the sum of arithmetic mean of the intensity in a group and the ratio of the positive/total multiplied by 2.

Statistical analysis

The results were expressed as mean ± SEM. Data were analysed using one way ANOVA followed by Tukey's multiple range test A 'p' value less than 0.05 was considered as statistically significant.

Results

Ethanol-induced gastric ulcer model

The results are summarized in Table 1. PCE showed significant dose dependent reduction in ulcer index at 300, 500 and 800mg/kg, when compared with the control group ($p< 0.05$). Similarly, cimetidine produced significant reduction in ulcer index as compared with control.

Aspirin-induced gastric ulcer model

As shown in Table 2, PCE treatment showed significant reduction in ulcer index when compared with the control group ($p< 0.05$). Positive control, cimetidine treated animals also showed significant reduction in ulcer index as compared to control animals ($p< 0.05$).

Pylorus ligation-induced gastric ulcer model

As shown in Table 3, PCE and cimetidine showed significant reduction in ulcer index ($p < 0.05$) as compared to control. None of the treatment groups showed any marked change in volume of gastric acid secretion parameter. There was significant rise in gastric pH by PCE and cimetidine as compared to control group (Table 3). The treatment groups viz. PCE and cimetidine showed significant reduction in total acidity when compared with the control group (Table 3). Total acid output remained unaltered in all the treatment groups. Along with total acidity, pepsin activity was significantly reduced by PCE and cimetidine treatment (Table 3). Significant rise in total carbohydrate content was observed in treatment groups as compared with the control

Treatment	Dose (mg/kg, p.o.)	Ulcer Index	% Protection
Control	-	2.19 ± 0.36	-
PCE	300	0.91 ± 0.14*	58.45
	500	0.59 ± 0.08*	73.06
	800	0.39 ± 0.08*	82.19
Cimetidine	100	1.17 ± 0.08*	46.58

n = 6 Expressed as mean ± SEM. One way Anova followed by Tukey's multiple range test; *p < 0.05 when compared with control group.

Table 1: Effect of PCE against ethanol–induced gastric ulcer model in rats.

Treatment	Dose (mg/kg, p.o.)	Ulcer index	% protection
Control	--	1.23 ± 0.08	-
PCE	500	0.62 ± 0.10*	49.59
Cimetidine	100	0.48 ± 0.04*	60.98

n = 6 Expressed as mean ± SEM. One way Anova followed by Tukey's multiple range test; *p<0.05 when compared with control group.

Table 2: Effect of PCE against aspirin-induced gastric ulcer model in rats.

Parameters	Control	PCE (500 mg/kg) (p.o.)	Cimetidine (100 mg/kg) (p.o.)
Ulcer index	0.66 ± 0.11	0.11 ± 0.03*	0.14 ± 0.05*
Vol. of gastric content (ml/100g)	3.67 ± 0.24	4.00 ± 0.56	4.15 ± 0.13
pH	2.20 ± 0.19	3.62 ± 0.19*	5.20 ± 0.07*
Total acidity (mEq/L)	14.77 ± 0.94	5.03 ± 0.33*	9.83 ± 0.20*
Total acid output (mEq/100 g)	54.04 ± 4.70	46.27 ± 15.3	40.22 ± 0.88
Pepsin activity (µg/ml)	750 ± 41.03	299.83 ± 17.62*	310.0 ± 31.97*

n= 6 Expressed as mean ± SEM. One way Anova followed by Tukey's multiple range test; *p<0.05 when compared with control group.

Table 3: Effect of PCE on ulcer index and acid secretory parameters in pylorus ligated gastric ulcers in rats.

Parameters	Control	PCE (500 mg/kg, p.o.)	Cimetidine (100 mg/kg, p.o.)
Total carbohydrate (µg/ml)	496.67 ± 46.69	1506.33 ± 100.16*	880.5 ± 54.45*
Protein content (µg/ml)	294.7 ± 67.04	129.5 ± 21.78*	46.17 ± 1.14*
TC : PR ratio	2.18 ± 0.41	13.64 ± 2.24*	19.08 ± 1.12*
GWMC	57.63 ± 7.90	59.18 ± 6.12	74.21 ± 7.99

n= 6 Expressed as mean ± SEM. One way Anova followed by Tukey's multiple range test; *p<0.05 when compared with control group.

Table 4: Effect of PCE on mucoprotective parameters in pylorus ligated gastric ulcer in rats.

Treatment	Ulcer incidence No %	Mortality No. %	Ulcer score	Total lesion area (mm^2)	Ulcer index	% inhibition
Control	8/8 100	3/8 37.5	2.50 ± 0.28	88.38 ± 3.87	4.5	-
PCE (500 mg/kg, p.o.)	8/8 100	1/8 12.5	1.00 ± 0.12	43.75 ± 1.79*	3.0	33.33
Cimetidine (100mg/kg, p.o.)	8/8 100	0/8 0.0	0.90 ± 0.12*	41.2 ± 3.04*	2.9	35.56

n= 6 Expressed as mean ± SEM. One way Anova followed by Tukey's multiple range test; *p<0.05 when compared with control group.

Table 5: Effect of PCE on cysteamine-induced duodenal ulcer in rats.

group (Table 4). At the same time, protein content was significantly reduced in both the treatment groups (Table 4). Based on the results of total carbohydrate and protein content, mucin activity was determined in terms of TC: PR ratio increased significantly as compared to control. Gastric wall mucous content was increased significantly in PCE treated group as compared to control (Table 4).

Cysteamine-induced duodenal ulcer model

In cysteamine-induced duodenal ulcer model, PCE and cimetidine showed significant reduction in the total lesion area when compared with control group (Table 5).

Discussion

50% ethanolic extract of patol churna showed significant antiulcer effect against ethanol and aspirin-induced gastric ulcers. Ethanol administration may evoke gastric secretion through a more direct action on the stomach, involving the release of gastrin, histamine [23] and endogenous endothelin (ET-1) from vascular endothelial cells in the fundic mucosa [24]. Also, certain prostaglandins are capable of protecting rats against gastric mucosal lesions caused by necrotizing agents like ethanol and strong acid [25]. Aspirin has been recorded to cause mucosal damage by several factors such as inhibiting prostaglandin synthesis, enhancing acid secretion, increasing back diffusion of H^+ ions, decreasing mucin secretion and breaking of mucosal barrier [26]. Thus, the antiulcer activity of the patol churna extract in these models can be related to the cytoprotective action.

Gastric hypersecretion plays an important role in production of experimental ulcers by pylorus ligation [27]. Increased biosynthesis of nucleic acids and increased metabolism of carbohydrates and thereby exhaustion of carbohydrates and other compensatory mechanisms could also be responsible for ulceration due to pylorus ligation [28]. It is evident from the biochemical parameters that PCE has antiulcer effect in pylorus ligation model. The mechanism of their antiulcer activity can be related to the acid neutralizing property, reduction in acid-pepsin secretion and increase in mucin activity.

Cysteamine-induced ulcers are considered to be due to continuous hypersecretion of gastric acid [29]. The pathogenesis of cysteamine-induced duodenal ulcers includes enhanced gastric acid secretion [29], increased duodenal motility [30], delayed gastric emptying [31] and decreased duodenal bicarbonate secretion in response to acid [31]. It is suggested from our results that patol churna and cimetidine possess significant antiduodenal ulcer activity. The mechanism of this activity can be related to inhibitory effect of acid and pepsin activity.

Conclusion

The results of the present study indicate that 50% ethanolic extract of patol churna has protective effect against experimental gastro-duodenal ulcers in rats.

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