

Gastric Antisecretory, Antiulcer and Cytoprotective Properties of Ethanolic Extract of *Alpinia galanga* Willd in Rats

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The effect of *Alpinia galanga* extract has been studied on experimentally induced gastric ulcers in rats. The ethanolic extract of *A. galanga* at a dose of 500mg/kg, significantly reduced the intensity of gastric mucosal damage induced by pyloric ligation and hypothermic restraint stress in rats. It produced a significant decrease in gastric secretion in pylorus ligated rats and a highly significant cytoprotective effect against 80% ethanol-, 0.6 M HCl-, 0.2 M NaOH- and 25% NaCl-induced cytodestruction. Pretreatment with the extract significantly prevented hypothermic stress-induced gastric wall mucus depletion. These findings suggest that a significant antisecretory and cytoprotective action of *A. galanga* may be responsible for its antiulcer activity.

Keywords: *Alpinia galanga*; gastric secretion; gastric ulcers; cytoprotection; gastric wall mucus.

INTRODUCTION

Alpinia galanga willd., a member of the zingiberaceae family, is commonly used in the Arabian and in Unani systems of medicine for the treatment of dyspepsia, gastralgia, chronic enteritis and sea sickness (Nadkarnai, 1954; Keys, 1985; Ageel, 1987). The rhizome is also said to promote digestion and is useful in the treatment of abdominal colic (Dymock, 1972). Mitsui *et al.* (1976) have isolated potent antiulcer principles from the seeds of *Alpinia galanga*. In China it is used for the treatment of stomach cancer (Perry, 1980). Other species of *Alpinia* have also been shown to possess antiulcer properties in rats (Wang *et al.*, 1972). A survey of the literature showed that no experimental data are available to justify the medicinal use of the rhizome of this plant in traditional medicine. In the present study an attempt has been made to carry out a preliminary investigation into the gastric antiulcer activity of *Alpinia galanga* in rats.

MATERIALS AND METHODS

Extract preparation. *A. galanga* rhizomes were procured from the local market of Riyadh, Saudi Arabia and identified in the Taxonomy Division of the Medicinal, Aromatic and Poisonous Plants Research

Center of King Saud University, Riyadh. The powdered drug (500 g) was extracted using a percolation method and 96% ethanol. The solvent was then removed at low temperature under reduced pressure, and the extracts were stored in a refrigerator for pharmacological studies. The extract yield was 5.6% (w/w) in terms of starting material. The dried extract was dissolved in water before administration to the animals.

Wistar albino rats of either sex, approximately of the same age, weighing 150-200 g, and fed on standard chow diet were used. They were divided into groups of six animals each. The distribution of animals in groups, the sequence of trials, and the treatments were randomized. The solutions of the ulcerogenic drugs and necrotizing agents were freshly prepared before administration. The animals were killed by ether euthanasia. The stomachs were removed, opened along the greater curvature, washed with saline and examined with a 6.4 x binocular magnifier. Lesions were also assessed by two observers unaware of experimental protocols. Gastric lesions induced by the drugs used in this study were multiple in each stomach. They were evaluated singly according to their dimensions and severity and scored between 0, no visible ulcers, and 10, deep lesion with diameter greater than 8 mm, in each stomach. The scores for each single lesion were then totaled. The results refer to average lesion score \pm SEM; statistical analysis of the severity of gastric ulcers was done by Student's *Mest*.

Gastric wall mucus determination. A slightly modified procedure of Corne *et al.* (1974) was followed. The

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glandular segments from stomachs which had been opened along their greater curvatures were removed and weighed. Each segment was transferred immediately to 10 mL of 0.1% w/v Alcian blue (dye) solution. Colour absorbance was recorded by means of a spectrophotometer (LKB) set at an optimal wave length of 596 nm. The quantity of Alcian blue extracted per g wet weight of glandular tissue was then calculated from standard curves.

Experimental gastric lesions

Pylorus ligated (Shay) rats. The animals were fasted for 48 h with access to water *ad libitum* before the pylorus was ligated under light anaesthesia, care being taken not to cause bleeding or to occlude blood vessels (Shay *et al.*, 1945). *A. galanga* extract was administered (i.p.) just after pylorus ligation. The animals were killed 6h after the pylorus ligation, the stomachs removed, contents collected and measured. Each stomach was examined for lesions.

Hypothermic restraint stress-induced ulcers. The method of Levine (1971) was followed with slight modification. The animals were fasted for 36 h with access to water *ad libitum* and, 1 h after the drug treatment, they were immobilized in restraint cages and placed in a ventilated refrigerator maintained at a temperature of -4°C for 2h. The animals were then killed and the stomachs were excised. They were examined for the severity of intraluminal bleeding according to the following arbitrary scale: 0, no blood detectable; 1, thin blood follows the rugae; 2, thick blood follows the rugae; 3, thick blood follows the rugae with blood clots in certain areas; and 4, extensive covering of the whole gastric mucosal surface with thick blood. After removing the blood, the lesions in each stomach were scored.

Indomethacin-induced gastric ulcers. Indomethacin was suspended in 1% carboxymethylcellulose in water (6 mg/mL) and administered p.o. at a dose of 30 mg/kg (0.5 mL/100 g) to rats fasted for 36 h (Bhargava *et al.*, 1973). *A. galanga* extract was administered 30min before indomethacin. The rats were killed 6h after indomethacin administration.

Reserpine-induced gastric ulcers. The method of Gupta *et al.* (1974) was followed. Reserpine (5 mg/kg i.m.) was administered to rats fasted for 36 h. The extract was administered 30 min before the administration of reserpine. The animals were killed 24 h later.

Necrotizing agent-induced gastric ulcers (cytoprotection studies). The experiments were carried out on male Wistar rats fasted for 36 h with access to drinking water *ad libitum*. The animals were given 1 mL of either 80% ethanol, 0.6 M HCl, 0.2 M NaOH, or 25% (w/v) NaCl p.o. The extract was administered 30 min before the necrotizing agents, and the animals were killed 1 h after the administration of necrotizing agents (Robert *et al.*, 1983).

RESULTS AND DISCUSSION

In Shay rats, ligation of pylorus for 6 h produced mild ulcers mainly located in the forestomach (Table 1). Pretreatment of animals with *A. galanga* extract significantly decreased gastric secretions and ulcers. The animals subjected to hypothermic restraint stress exhibited intraluminal bleeding, depletion of gastric mucosal wall and ulceration, mainly in the glandular segment of the stomach (Table 2). Treatment of animals with the extract of *A. galanga* showed significant protective effect on stress-induced changes in gastric mucosa. The antiulcer activity in these models might be attributed to an antisecretory effect of the extract. In human subjects also, the *A. galanga* has been reported to relieve the symptoms of heart burn and dyspepsia (Ageel *et al.*, 1987). The increase in

Table 1. Effect of ethanolic extract of *Alpinia galanga* on the gastric secretion and ulcer index in 6 h pylorus ligated (Shay) rats

Treatment	Dose (mg/kg)	Volume of gastric secretion	Ulcer index (mean \pm SE)
Control		9.41 \pm 1.09	2.0 \pm 0.06
<i>Alpinia galanga</i>	500	6.16 \pm 0.41*	0.16 \pm 0.00°

Six animals were used in each test group.

* $p < 0.05$ (Student's *t*-test).

Table 2. Effect of ethanolic extract of *Alpinia galanga* on gastric wall mucus changes in rats

Groups	Dose (mg/kg p.o.)	Gastric wall mucus (tig Alcian blue/g wet glandular tissue)	Intraluminal bleeding (mean score \pm SE.)	Ulcer index
Normal unstressed		310.74 \pm 30.78= (7)		
Hypothermic stressed		200.72 \pm 10.05 (7)	2.50 \pm 0.56 (6)	31.2 \pm 2.40 (6)
Hypothermic stressed + <i>Alpinia galanga</i>	500	360.04 \pm 40.99 (7)	0.66 \pm 0.49" (6)	19.8 \pm 3.71* (6)

Numbers in parentheses indicate the number of animals used.

" Compared with the stressed (control) group.

* $p < 0.05$ (Student's *t*-test).

gastric secretion has been considered as a pathogenic mechanism responsible for stress-induced gastric lesions (Brodie *et al.*, 1962; Murakami *et al.*, 1985). The gastric lesions induced by various necrotizing agents including ethanol, HCl, NaOH and NaCl, produced patchal ulcers of various size, usually parallel to the major axis of the stomach. The intensity of the ulcers was significantly reduced in the animals treated with *A. galanga* extract (Table 3). These findings argue for a 'cytoprotective' effect of *A. galanga* extract according to the definition of Robert (1979). The necrotizing agents produce ulceration in gastric mucosa by depleting gastric mucus and breaking the mucosal barrier (Davenport, 1967). The ability of *A. galanga* extract to inhibit gastric mucus depletion, as observed in our study, might be responsible for increasing mucosal resistance against noxious chemicals (Koo *et al.*, 1986). The gastric mucus coat is thought to be important in both preventing damage and in facilitating the repair of gastric epithelium (Wallace and Whittle, 1986). However, pretreatment of animals with *A. galanga* extract did not protect the gastric mucosa against

Table 3. Effect of ethanolic extract of *Alpinia galanga* against the gastric lesions induced by various necrotizing agents in rats

Procedure	Ulcer index mean \pm SE	
	Control	<i>Alpinia galanga</i> (500mg/kg p.o.)
80% Ethanol	7.16 \pm 0.3	0.16 \pm 0.16*
0.6 M HCl	7.16 \pm 0.4	1.50 \pm 0.34*
0.2 M NaOH	7.16 \pm 0.4	0.33 \pm 0.21*
25% NaCl	6.83 \pm 0.83	0.33 \pm 0.21*

Six animals were used in each group.

* $p < 0.001$, Student's t-test as compared to respective controls.

Table 4. Effect of ethanolic extract of *Alpinia galanga* on gastric mucosal damage induced by indomethacin and reserpine

Treatment	Dose (mg/kg p.o.)	Ulcer index (mean \pm SE)	p value (Student's t-test)
Indomethacin			
Control		35.66 \pm 3.49	
<i>Alpinia galanga</i>	500	29.33 \pm 3.85	$p > 0.05$
Reserpine			
Control		40.66 \pm 1.11	
<i>Alpinia galanga</i>	500	26.83 \pm 3.19	$p > 0.05$

Six animals were used in each group.

indomethacin and reserpine (Table 4). The failure of the extract to protect against gastric ulceration induced by indomethacin clearly excludes a prostaglandin mediated protective mechanism. However, Kuichi *et al.* (1982) have isolated three new diarylhepatonoids, inhibitors of prostaglandin biosynthesis, from *Alpinia officinarum*, a close species of *Alpinia galanga*. The phytoconstituents of the rhizome of *Alpinia galanga* responsible for antiulcer activity are not known. The seeds of this plant have been reported to contain two highly active components, namely acetoxychavicol and acetoxyeugenol (Mitsui *et al.*, 1976). In Taiwan, antiulcer biopharmaceuticals have been derived from *Alpinia speciosa* (Wang *et al.*, 1972). Further studies on the isolation of antiulcer compounds from the rhizomes of *Alpinia galanga* are suggested.

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