

The Effect of *Opuntia ficus-indica* var. *saboten* Fruit on Gastric Lesion and Ulcer in Rats

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Abstract – The effects of the dried fruit powder of *Opuntia ficus-indica* var. *saboten* (OF-f) were investigated on gastric lesion and ulcer models in rats. It showed significant inhibition in HCl-ethanol and HCl-aspirin induced gastric lesion at a dose of 600 mg/kg, *p.o.* OF-f also showed significant inhibition in indomethacin induced gastric lesion at the doses of 200 and 600 mg/kg, *p.o.* However, it did not affect aspirin and Shay ulcer in rats. It also did not affect the gastric juice secretion, acid output and pH. These data suggest that OF-f possesses pronounced inhibitory action on gastric lesion of rats.

Key words – *Opuntia ficus-indica* fruit, Cactaceae, antigastric lesion, antigastric ulcer.

Introduction

The *Opuntia ficus-indica* var. *saboten* Makino (Cactaceae) is a tropical or subtropical plant in origin which has now been cultivated in Jeju Island, Korea. Its fruit and stem have been used in Jeju area as folk medicine for burns, edema, cough, gastritis, diabetes and asthma. The compositions of its fruit (Lee *et al.*, 1997) were reported, and isolation of flavonoids (Jeong *et al.*, 1999), and pridic acid (Impellizzeri and Piattelli, 1972) were also reported. Recently, monoamine oxidase B inhibitors were isolated from *O. ficus-indica* fruit (Han *et al.*, 2001). It was also reported that the ethanol extract of the fruit had inhibitory effects on carrageenan-induced paw edema and leukocyte migration in CMC pouch in rats (Park *et al.*, 1998). An ethanol extract of the fruit had protective effect only against HCl-ethanol induced gastric lesion (Park *et al.*, 1998). This study deals with the effectiveness of *O. ficus-indica* fruit on various gastric lesion and ulcer models in rats.

Materials and Methods

Plant material and chemicals – *O. ficus-indica* fruit cultivated in the Cheju island was used. The fruits were cut in pieces, lyophilized and ground into powder. The powder (OF-f) for this study was made at Pukjeju Agricultural Development and Technology

Extension Center. Total yield of OF-f used for the test corresponded to 8±0.5% from the raw material. This substance OF-f was used as a test sample. Ranitidine (Union Quimico Farmaceutica S.A. Spain) and indomethacin (Sigma Chemical Co.) were used. Other drugs used were either pharmaceutical or reagent grade.

Animals – Male Sprague-Dawley rats were supplied from breeding facilities of Natural Products Research Institute, Seoul National University. Solid food (Samyang Yuji Co. Ltd.) and tap water were provided *ad libitum*. All animals were housed for 1 week in a controlled 12 hr light-dark environment at 22±1°C. The substance was suspended in 0.5% CMC in distilled water and a volume of 0.5 ml/100 g (b.w.) was administered. Control group received only 0.5% CMC solution.

HCl-ethanol induced gastric lesion – The experiment was performed according to the method of Mizui and Dodeuchi (1983). Briefly, rats (180-200 g) were fasted for 24 hr with free access to water before experiment. HCl-ethanol (60% ethanol with 150mM HCl) solution in a volume of 0.5 ml/100 g was orally administered. One hr later, the animals were sacrificed with ether and each stomach was excised. Then, 12ml of 2% formalin was infused into the stomach, and the stomach was soaked in 2% formalin for 10 min. The stomach was incised along the greater curvature and examined for the presence of gastric lesion in the glandular portion. The length of each lesion (mm) was measured under the dissecting

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microscope (10 \times), and total value was expressed as a lesion index. The substance was given orally 30 min prior to administration of HCl-ethanol solution.

HCl-aspirin induced gastric lesion – According to the method of Guth *et al.* (1979), rats (180-200 g) were fasted for 24 hr with free access to water before experiment. The animals were given orally 150 mM HCl with aspirin 200 mg/kg suspended in 5% gum acacia in a volume of 0.5 ml/100 g. One hr later, the animals were sacrificed and each stomach was excised and fixed with formalin solution as described above and the lesion index was measured. The substance was given orally 30 min prior to administration of HCl-aspirin solution.

Indomethacin induced gastric lesion – According to the method of Suzuki *et al.* (2000), rats (180- 200 g) were fasted for 24 hr with free access to water before experiment. The substance was orally given and 30 min later indomethacin 35 mg/kg suspended in 0.5% CMC was injected subcutaneously. The animals were sacrificed 7 hr after indomethacin injection and the excised stomach was treated as described above and the area (mm²) of hemorrhagic lesion developed in the corpus mucosa was measured.

Aspirin induced gastric ulcer – According to the method of Okabe *et al.* (1974), rats (200-220 g) were fasted for 24 hr with free access to water before experiment. The pylorus of each animal was ligated under ether anesthesia. The substance was given by intragastrically after pylorus-ligation. Ten min later, aspirin 150 mg/kg suspended in 0.5% CMC was administered orally in a volume of 0.5 ml/100 g. Seven hr after aspirin treatment, the animals were sacrificed and each excised stomach was treated as described above and glandular portion was examined to evaluate the ulcers.

Shay ulcer – Rats (210-230 g) were fasted for 36 hr with free access to water prior to the experiment. The pylorus of each animal was ligated under ether anesthesia as described by Shay *et al.* (1945). The substance was given intraduodenally immediately after pylorus-ligation. Fifteen hr later, the animals were sacrificed and the excised stomach was treated as described above and examined for gastric ulcers in the forestomach. The area of each ulcer was measured and summed. The ulcer index was graded from 1 to 5 according to the size of the area; i. e., 1-10 mm² as 1, 11-20 mm² as 2, 21-30 mm² as 3, 31-40 mm² as 4, 41-50 mm² as 5 or perforated cases as 5 (Takagi *et*

al., 1974).

Gastric secretion – Rats (220 g) were fasted for 24 h with free access to water before the experiment. The animals were anesthetized with ether and the pylorus was ligated by method of Shay *et al.* (1945). The substance was given intraduodenally immediately after pylorus-ligation. Four hr later, the animals were sacrificed and the stomach was excised. The contents of stomach were collected and centrifuged at 3000 rpm for 10 min. Total volume, pH, acidity and acid output of the supernatant were measured. The acidity were determined by titration of the gastric juice with 0.05N NaOH using phenolphthalein as an indicator.

Statistical analysis – All data represent means \pm S.E. Statistical analyses of the data were performed using analysis of variance followed by Student's *t*-test. All data were evaluated at the $p < 0.05$ level of significance.

Results

HCl-ethanol induced gastric lesion – As shown in Fig. 1, the lesion index of control group is 98.2 and OF-f at a dose of 600 mg/kg, *p.o.* showed significant inhibition by 71.8%. Ranitidine at 50 mg/kg showed 78.5% inhibition.

HCl-aspirin induced gastric lesion – As shown in Fig. 2, OF-f at a dose of 600 mg/kg, *p.o.* showed significant inhibition by 76.6%. Ranitidine at 50 mg/kg showed 71.1% inhibition.

Indomethacin induced gastric lesion – The effect of OF-f on indomethacin induced gastric lesion was represented in Fig. 3. It showed significant inhibition at the doses of 200 and 600mg/kg, *p.o.* by 44.1%

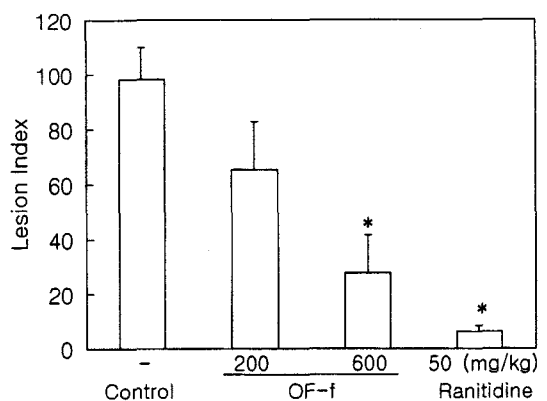


Fig. 1. Effect of OF-f on HCl-ethanol induced gastric lesion. * $p < 0.05$; Significantly different from the control group (n=8).

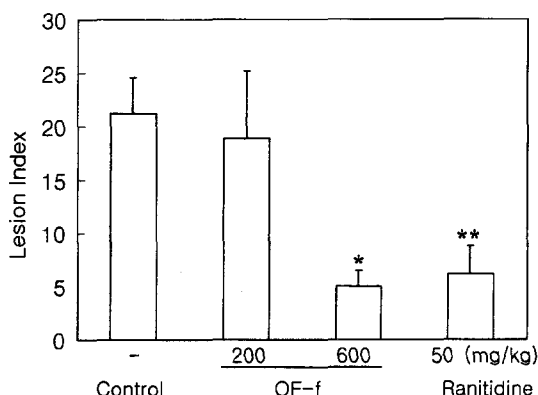


Fig. 2. Effect of OF-f on HCl-aspirin induced gastric lesion. * $p < 0.01$, ** $p < 0.001$; Significantly different from the control group (n=8).

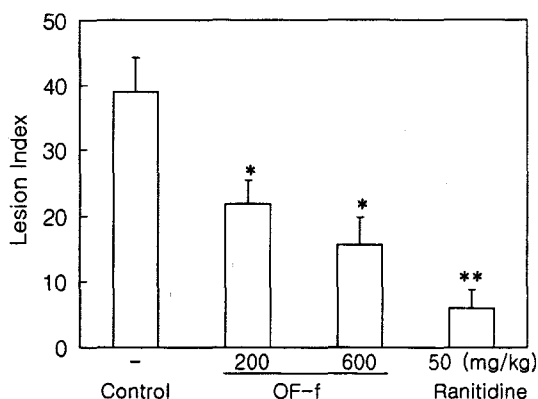


Fig. 3. Effect of OF-f on indomethacin induced gastric lesion. * $p < 0.01$, ** $p < 0.001$; Significantly different from the control group (n=8).

and 60%, respectively. Ranitidine at 50 mg/kg showed 86.4% inhibition.

Aspirin induced gastric ulcer – As shown in Fig. 4, OF-f at the intragastric doses of 200 and 600 mg/kg did not show inhibition of the ulcer.

Shay ulcer – As shown in Fig. 5, OF-f at the

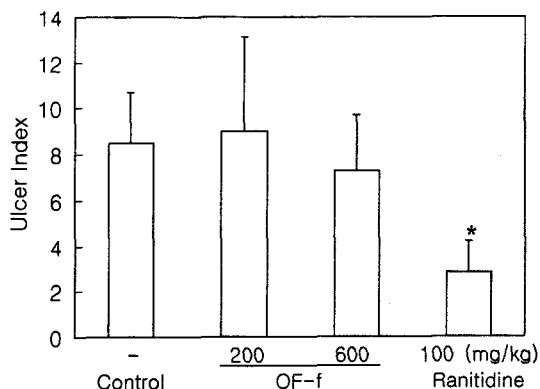


Fig. 4. Effect of OF-f on aspirin induced gastric ulcer. * $p < 0.01$; Significantly different from the control group (n=8).

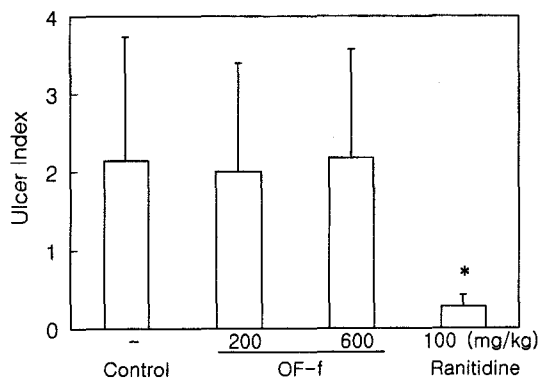


Fig. 5. Effect of OF-f on Shay ulcer. * $p < 0.01$; Significantly different from the control group (n=8).

intraduodenal doses of 200 and 600 mg/kg did not affect the ulcer.

Gastric secretion – The effect of OF-f on gastric secretion in rats is shown in Table 1. OF-f at 200 and 600 mg/kg given intraduodenally did not affect the volume of gastric acid secretion, acid output and pH, while ranitidine at 50 mg/kg showed significant inhibition of acid secretion and acid output and increases in pH.

Table 1. The effect of OF-f on gastric secretion

| Treatment | Dose (mg/kg, <i>i.d.</i>) | No. of animals | Gastric volume (ml) | pH | Acidity (eq/ml) | Acid output (eq/ml/4hrs) |
|------------|----------------------------|----------------|---------------------|-----------|-----------------|--------------------------|
| Control | – | 8 | 4.86±0.9 | 1.2±0.1 | 116.1±5.5 | 589.6±122 |
| OF-f | 200 | 8 | 3.21±0.2 | 1.4±0.1 | 106.4±5.4 | 325.0.3±41 |
| | 600 | 8 | 3.51±0.4 | 1.4±0.1 | 110.0±7.0 | 399.3±69 |
| Ranitidine | 50 | 8 | 1.91±0.3* | 5.7±0.9** | 90.9±11* | 198.9±22* |

* $p < 0.05$, * $p < 0.01$; Significantly different from the control group.

Discussion

Effects of OF-f on three models of gastric lesion and two models of gastric ulcer in rats were investigated. OF-f showed significant inhibition on HCl-ethanol, HCl-aspirin and indomethacin induced gastric lesions. Similarly, the ethanol extract of *O. ficus-indica* fruit was reported to have positive activity on HCl-ethanol induced gastric lesion (Park *et al.*, 1998). HCl-ethanol and HCl-aspirin induced lesions are known to be produced by direct irritation of gastric mucosal barrier (Seiki *et al.*, 1990). Thus the effectiveness of OF-f on these gastric lesions might be related to direct protection of the irritation. OF-f also showed effect on indomethacin induced gastric lesion. Takeuchi *et al.* (1986) reported that an increase of gastric motility in rats may play a role in the pathogenesis of lesion induced by indomethacin. However, the effectiveness is unknown at present except cytoprotective effect.

OF-f did not affect aspirin induced and Shay ulcer, and also did not affect the volume of gastric acid secretion, acid output and pH. It is indicated that the negative anti-ulcer activity of OF-f might be related to no effects on gastric acid secretion. In conclusion, it is suggested that OF-f possesses pronounced inhibitory action on gastric lesion, but does not have anti-ulcer activity in rats.

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