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Inhibition of Experimental Gastric Ulcer by Potato Tubers and the Starch

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Abstract – In an attempt to establish anti-ulcerogenic activity of potato tubers, inhibitory activity against ethanol- and indomethacin-induced gastric ulcer models in rats was evaluated for the first time. From several varieties of potato tubers including *Solanum tuberosum* L. cv. Superior (white skin and fresh potato) and two new varieties of (Bora valley and Gogu valley), raw potato juice was prepared and the starch was obtained from each juice by filtration and drying. Upon oral administration to rats, raw potato juice showed more or less inhibitory activity. The starch showed higher and dose-dependent inhibitory activity, suggesting that the active ingredient in raw potato juice may be the starch. Particularly, the starch obtained from the tubers of new potato variety, “Bora valley,” with purple color, showed the highest inhibitory activity (62.4% and 37.1% inhibition of ulcer index at 500 mg/kg), while omeprazole (proton pump inhibitor) used as a reference drug showed 74.4% and 75.7% inhibition at 20 mg/kg against ethanol- and indomethacin-induced ulcer formation, respectively. The present study provides a first evidence of anti-ulcerogenicity of raw potato juice and the starch. Especially, the starch from “Bora valley” strongly inhibited ulcer formation in rats. Considering that these are food components, they may be safely used for anti-ulcerogenic nutraceuticals.
Keywords – Potato, *Solanum tuberosum* L. cv. Bora valley, Fresh juice, Starch, Ethanol-induced ulcer, Anti-ulcerogenicity

Introduction

Potato (*Solanum tuberosum* L.) is one of major crops consumed worldwide. Generally, potato has not been regarded as a food having high pharmacological activity. However, some potato may have significant and meaningful biological activities depending on the genotypes. Accordingly, many new varieties have been developed recently and their new usages are actively searched.

Previously, several pharmacological activities of potato tubers and their constituents have been described. For example, potato extract exhibited anticancer activity (de Lorenzo *et al*., 2001). Potato ingestion improved cholesterol metabolism (Robert *et al*., 2006). Among the constituents, potato starch showed beneficial effects on postprandial glycemia and energy expenditure (Raben *et al*., 1994; Tagliabue *et al*., 1995). Potato starch has been also reported to ameliorate colonic and inflammatory bowel diseases (de Deckere *et al*., 1995; Kleessen *et al*., 1997; Jacobasch *et al*., 1999; Martinez-Puig *et al*., 2003; Nofrarias *et al*., 2007). Besides, there is a belief in some countries that ingestion of raw potato juice could provide beneficial effect on gastritis and gastric ulcer. However, no report has been described to prove this pharmacological activity to date. It was only demonstrated that one form of potato protein hydrolysate protected from ethanol-induced gastric mucosal damage (Kudoh *et al*., 2003). Here, an attempt has been made to establish anti-ulcer action of potato for the first time. The potato tubers examined include *S. tuberosum* L. cv. Superior (white potato) and two new varieties (Bora valley and Gogu valley). Bora valley was registered as national potato variety in 2004 after testing two years of evaluation by government research institute. Bora valley was derived from traditional breeding method and has been distributed to other countries such as Russia, USA, Canada, France, Nepal, India, China, Kazakhstan etc. Gogu valley has been bred newly and in the process of national variety registration. Bora valley was developed for the purple potato chip, baking, and raw eating purpose, and Gogu valley is raw eating potato (salad) like sweet potato after cold storage. In this study, the anti-ulcerogenicity, especially, anti-ulcer activity of the starch portion was described.

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Experimental

Chemicals – Absolute ethanol was obtained from Merck Co. (Germany). Carboxymethyl cellulose (CMC), indomethacin and omeprazole (reference drug) were obtained from Sigma-Aldrich Chem. (St. Louis, MO). Commercial potato starch consisting of potato starch and small amount of corn starch was purchased from local market. From sweet potato obtained from local market, the starch was prepared using the same experimental procedure described below. Vegetable juice made of mixed vegetables (Pulmuwon Co., Seoul, Korea) was also used as a reference.

Animals – Male Sprague-Dawley (SD) rats (specific pathogen-free, 4 weeks) were purchased from Orient-Bio Co. (Korea). Animals were housed in a specific pathogen-free animal fertility under the conditions of 20 - 22 ^oC, 40 - 60% relative humidity and 12 h/12 h light/dark cycle. Animals were fed with standard Lab. Chow (Purina Korea) and water *ad libitum* at least for 7 days prior to experiment.

Potato tubers – Potato tubers including the white potato (*S. tuberosum* L. cv. Superior, also called as "Sumi", KPGR-K54) and newly developed potato varieties (Bora valley, KPGR-V20, and Gogu valley, KPGR-V1) were provided from the Center of the Korea Potato Genetic Resources (KPGR) II, Kangwon National University (Chunchon, Korea). Each potato was minced in a juicer and the fresh juice was collected. To obtain raw potato starch, the fresh juice was filtered after remaining at room temperature for 10 min. Potato starch was dried at 60 ^oC for 2 days. In general, 100 - 140 mg potato starch (based on dry weight) was obtained from 1 ml of raw potato juice. Raw potato juice, the filtrate and dried potato starch were used throughout this study.

Ethanol-induced ulcer formation in rats – Animals were caged in 6 animals per group. Prior to experiments, animals were fasted overnight (12 h). Test samples including a reference compound (omeprazole) dissolved in 0.1% CMC were orally administered. One hour later, absolute ethanol (0.5 ml) was orally administered. Four hours later, the rats were sacrificed and the stomach was excised. The excised tissues were fixed in 2% formalin solution. After drying, ulcer area was measured by image analysis system of ITPlus (Sometech Inc., Korea) under a dissecting microscope. Data were represented as ulcer area (mm^2) and ulcer index (ulcer area/stomach area).

Indomethacin-induced ulcer formation in rats – To the fasted rats (6 animals/group), the starch and a reference compound (omeprazole) dissolved in 0.1% CMC were orally administered. One hour later, indomethacin (40 mg/kg) dissolved in tween 80 (0.5 ml) was orally administered. Four hours later, the rats were sacrificed and the stomach was excised. And ulcer area was measured as described above.

Statistical analysis – Experimental values were represented as arithmetic mean ± SD. Unpaired Student's *t*-test was used to determine the statistical significance.

Results

Oral ethanol administration to rats produced gastric ulcer in 4 h. Ulcer area was measured and the ratio of ulcer area/total stomach area was regarded as ulcer index. In this animal model, ulceroprotective activities of raw potato juice, the filtrate and the starch of potato tubers of "Superior" (white potato) and "Bora valley" (purple potato), were compared. As demonstrated in Table 1, raw potato juice, the filtrate and the starch of "Bora valley" showed anti-ulcerogenicity, while raw potato juice from "Superior" showed marginal activity and the starch showed moderate inhibition. It is necessary to emphasize

Table 1. Inhibition of ulcerogenicity by potato tubers in rats

Treatment	Dose (mg/kg or ml/kg)	Ulcer area (mm^2)	Ulcer index (× 100) (ulcer area/total area)
Ethanol-treated	–	7.6 ± 3.6	1.19 ± 0.57
Omeprazole	20 mg	1.7 ± 3.9* (77.6)	0.21 ± 0.46* (82.4)
"Superior" juice	2.5 ml	7.1 ± 2.2 (6.6)	1.28 ± 0.38 (–)
"Superior" filtrate	2.5 ml	8.8 ± 2.4 (–)	1.45 ± 0.35 (–)
"Superior" starch	250 mg	4.9 ± 2.7 (35.5)	0.90 ± 0.45 (24.4)
"Bora valley" juice	2.5 ml	4.1 ± 0.8 (46.1)	0.86 ± 0.11 (27.7)
"Bora valley" filtrate	2.5 ml	4.6 ± 3.9 (39.5)	0.88 ± 0.64 (26.1)
"Bora valley" starch	250 mg	1.8 ± 0.8* (76.3)	0.29 ± 0.14* (75.6)

Arithmetic mean ± SD (n = 6), Values in parenthesis represent % inhibition of ulcerogenicity. *: P < 0.05, significantly different from the ethanol-treated group by unpaired Student *t*-test.

Table 2. Inhibition of ulcerogenicity by the starch from potato tubers of "Bora valley" in rats

Treatment	Dose (mg/kg)	Ulcer area (mm^2)	Ulcer index (× 100) (ulcer area/total area)
Ethanol-treated	–	17.3 ± 4.5	2.34 ± 0.87
Omeprazole	20	4.2 ± 3.0* (75.7)	0.60 ± 0.17* (74.4)
"Bora valley" starch	31.3	14.0 ± 10.3 (19.1)	1.45 ± 1.04 (38.0)
	125	12.4 ± 1.2 (28.3)	1.33 ± 0.42 (43.2)
	500	6.4 ± 6.0* (63.0)	0.88 ± 0.73* (62.4)

Arithmetic mean ± SD (n = 6), Values in parenthesis represent % inhibition of ulcerogenicity. *: $P < 0.05$, significantly different from the ethanol-treated group by unpaired Student *t*-test.

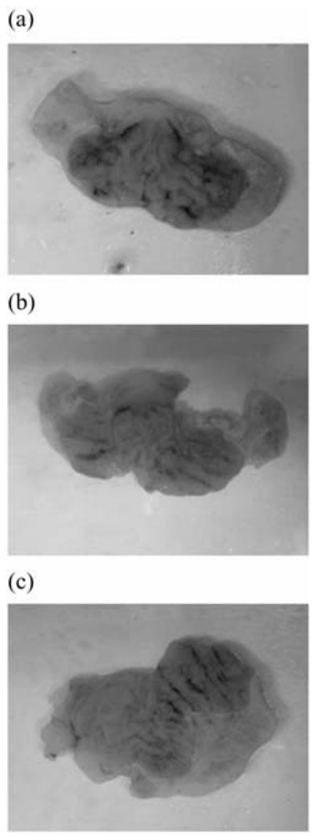

Fig. 1. Photographs of the ulcerogenic lesions
(a) Ethanol-treated control (b) omeprazole-treated (20 mg/kg) (c) The starch from "Bora Valley"-treated (500 mg/kg).

that potato variety of "Bora valley" showed much higher anti-ulcerogenicity than "Superior" variety. Especially, the starch of both potato varieties gave higher activity. The dose of the starch administration (250 mg/kg) used in this experiment is almost equal to or slightly less than the amount of the starch in raw potato juice (2.5 ml/kg). Therefore, it is reasonably thought that the major active constituent showing anti-ulcerogenicity in raw potato juice may be the starch, at least in part. Indeed, the starch from "Bora valley" tuber showed a dose-dependent inhibition of ulcer formation as demonstrated in Table 2, although its potency was far less than that of omeprazole. Omeprazole (proton pump inhibitor) used as a reference drug showed strong inhibitory activity at 20 mg/kg, p.o., as expected. The less severe ulcer formation of the lesions treated with omeprazol and the starch from "Bora valley" was represented in Fig. 1. In order to confirm the selective ulceroprotective activity of the starch from "Bora valley", anti-ulcerogenicity of commercial potato starch, sweet potato starch and mixed vegetable juice was compared. Table 3 demonstrated that these products showed only marginal or no activity, indicating that only the starch from "Bora valley" selectively and strongly inhibits ulcer formation induced by ethanol.

Next, the relative anti-ulcerogenicity of "Bora valley" and "Gogu valley" potato tubers was compared. At a dose of 2.5 ml/kg, the raw juice from "Bora valley" showed

Table 3. Inhibition of ulcerogenicity by starch from potato and sweet potato in rats

Treatment	Dose (mg/kg or ml/kg)	Ulcer area (mm^2)	Ulcer index (× 100) (ulcer area/total area)
Ethanol-treated	–	12.4 ± 9.0	1.66 ± 0.90
Omeprazole	20 mg	2.0 ± 1.4* (83.9)	0.35 ± 0.24* (78.9)
"Bora valley" starch	100 mg	7.0 ± 3.5 (43.5)	1.07 ± 0.61 (35.5)
Commercial potato starch	100 mg	9.5 ± 5.4 (23.4)	1.38 ± 1.02 (16.9)
Sweet potato starch	100 mg	11.8 ± 16.6 (4.5)	2.17 ± 2.46 (–)
Mixed vegetable juice	2.5 ml	12.7 ± 7.2 (-)	1.72 ± 0.64 (–)

Arithmetic mean ± SD (n = 6), Values in parenthesis represent % inhibition of ulcerogenicity. *: $P < 0.05$, significantly different from the ethanol-treated group by unpaired Student *t*-test.

Table 4. Inhibition of ulcerogenicity by raw potato juice and the starch of two potato varieties

Treatment	Dose (mg/kg or ml/kg)	Ulcer area (mm^2)	Ulcer index (× 100) (ulcer area/total area)
Exp. 1			
Ethanol-treated	–	18.7 ± 14.5	3.0 ± 2.6
Omeprazole	20 mg	8.2 ± 3.8 (56.1)	1.28 ± 0.47 (57.0)
“Bora valley” juice	2.5 ml	9.4 ± 2.9 (49.7)	1.67 ± 0.52 (44.3)
“Gogu valley” juice	2.5 ml	18.0 ± 3.7 (3.7)	2.98 ± 0.53 (0.7)
Exp. 2			
Ethanol-treated	–	14.6 ± 4.3	3.08 ± 1.91
Omeprazole	20 mg	6.4 ± 1.8* (56.2)	1.43 ± 0.48 (53.6)
“Bora valley” starch	125 mg	10.6 ± 5.3 (27.4)	2.0 ± 1.05 (35.1)
“Gogu valley” starch	125 mg	32.0 ± 16.8 (-)	5.84 ± 3.09 (-)

Arithmetic mean ± SD (n = 6), Values in parenthesis represent % inhibition of ulcerogenicity. *: P < 0.05, significantly different from the ethanol-treated group by unpaired Student *t*-test.

Table 5. Inhibition of indomethacin-induced ulcerogenicity in rats

Treatment	Dose (mg/kg)	Ulcer area (mm^2)	Ulcer index (× 100) (ulcer area/total area)
Indomethacin-treated	–	6.5 ± 2.1	1.25 ± 0.46
Omeprazole	20	1.6 ± 1.7* (75.9)	0.30 ± 0.35* (75.8)
“Bora valley” starch	31.3	6.4 ± 4.8 (1.1)	1.21 ± 0.77 (2.4)
	125	5.3 ± 4.1 (17.8)	1.09 ± 1.01 (12.4)
	500	3.5 ± 1.3* (44.4)	0.78 ± 0.26 (37.1)

Arithmetic mean ± SD (n = 6), Values in parenthesis represent % inhibition of ulcerogenicity. *: P < 0.05, significantly different from the indomethacin-treated group by unpaired Student *t*-test.

considerable inhibition as expected, while the raw juice from Gogu valley showed negligible effect against ulcer formation (Table 4). The similar patterns of anti-ulcerogenicity were also obtained from the starch of potato varieties. The starch from “Bora valley” inhibited ulcer formation whereas the starch from “Gogu valley” did not. All these results strongly indicated that high anti-ulcerogenicity is not a general pharmacological action of the starch from all potato tubers.

In order to establish anti-ulcerogenicity against other animal model, the starch from “Bora valley” was tested in indomethacin-induced ulcer formation. Treatment of indomethacin produced gastric ulcer (Table 5), although the ulcer index was lower than that of ethanol-induced ulcer. In this model, the starch from “Bora valley” also inhibited ulcer formation dose-dependently.

Discussion

The present investigation is the first report demonstrating the gastroprotective effect of raw potato juice and the starch. And it is strongly suggested that major active constituent in the juice may be the starch. Particularly, the starch from “Bora valley” possesses strong and selective anti-ulcerogenicity against ethanol- and indomethacin-induced ulcer formation in rats. Other starchs such as commercial potato starch, the starchs from other potato variety and sweet potato did not show strong inhibitory activity on ulcer formation. However, the reason for the differences of anti-ulcerogenicity among the starchs from different potato tubers is not understood at present. There should be some physico-chemical differences among the starchs to provide different anti-ulcerogenicity. This point and their action mechanism (s) remain to be further investigated.

The starch from white bread and cornflakes is digested in the small intestine (Englyst *et al*., 1985), while native potato starch is resistant to hydrolysis, called resistant starch (Fuwa *et al*., 1980). Raw resistant potato starch has been reported to have a beneficial effect on colonic and inflammatory bowel diseases (de Deckere *et al*., 1995; Kleessen *et al*., 1997; Jacobasch *et al*., 1999; Martinez-Puig *et al*., 2003; Nofrarias *et al*., 2007). Its action is demonstrated to be due to the fermentation in large intestine and production of short-chain fatty acids, ameliorating colonic disorders and reducing energy absorption. The present investigation may provide another useful and important pharmacological action of potato starch, gastroprotective activity.

In conclusion, potato tubers were evaluated for their anti-ulcerogenic potential using rat models of ethanol- and indomethacin-induced ulcer. Although the potencies were lower than that of clinically used drug, omeprazole, raw potato juice and the starch, especially from "Bora valley", considerably inhibit gastric ulcer formation. As food components, they may be safely used for anti-ulcerogenic nutraceuticals.

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