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Purgative Activities of Seunggitangs

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Abstract – The purgative activity of Seunggitang prescriptions (Deseunggitang, Soseunggitang and Joweseunggitang) was measured to compare the laxative potency of these herbal prescriptions. Daeseunggitang and Jowiseunggitang more potently stimulated the transportation of small and large intestine than Rhei Rhizoma alone. However, the small and large intestine transportation activities of Soseunggitang were similar to those of Rhei Rhizoma alone. Soseunggitang inhibited nitrite production in LPS-induced RAW 264.7 cells and trypsin than the other Seunggitangs. The inhibitory activity of Jowiseunggitang was more potent on nitrite production in LPS-induced RAW 264.7 cells than those of Daeseunggitang. These results suggest that Daeseunggitang can be used as a emergent purgative for patients with severe fever and constipation, Soseunggitang can be as a mild purgative for chronic constipation with inflammation and Jowiseunggitang can be as a potent purgative for patients for severe constipation and weak colitis.

Key words – Daeseunggitang, Soseunggitang, Joweseunggitang, purgative, nitrite

Introduction

Seunggitangs are representative purgatives in traditional Chinese medicine (Heo, 1966). The representative Seunggitangs are Daeseunggitang, Soseunggitang and Jowiseunggitang (Table 1). Dongwebogam (1966) describes that Daeseunggitang could be used in urgency or serious conspitation, Soseunggitang could be in less urgent syndromes than Daeseunggitang, and Jowiseunggitang could be in conspitations with febrile symptoms, which caused inflammation in intestine. Even if the application of these herbal formulae were theoretically different in Oriental medicine, the use of these formulae was clinically confused due to the deficiency of the experimental study. Thus, it is difficult to select Seunggitangs in Oriental clinicis for constipation patients with diverse syndromes.

Therefore, we studied in vivo purgative actions of Seunggitangs to provide the criteria to select proper herbal formula according to the syndromes of patients with constipation.

Materials and Methods

Materials – Rhei Rhizoma (roasted with alcohol), Magnoliae Cortex, Ponciri Fructus, Sodii Sulfas, Glycyrrhizae Radix (roasted) were purchased from Kyung Dong Market and identified by Dr. Nam-Jae Kim (East-West Medical Research Institute, Kyung Hee Univ.). The botanical identity of these herbal medicines was vouched in College of Pharmacy, Kyung Hee University (Seoul, Korea). *Escherichia coli* KCCM12451 and *Staphylococcus aureus* KCCM12103 were purchased from Korea Culture Collection of Microorganisms (Seoul, Korea). The other chemicals were of analytical reagent grade.

Extraction of samples – Each Seunggitang is prescribed in accordance with Dongwebogam and extracted with water. To extract Daeseunggitang, 30 g Magnoliae Cortex and 30 g Ponciri Fructus were extracted with 1000 ml water in a boiling water bath for 2 h, then add 60 g Rhei Rhizoma, boiled for 1 h and finally added 30 g Sodii Sulfas. The supernatant was used for animal experiment. To extract Soseunggitang, 22.5 g Magnoliae Cortex and 22.5 g Ponciri Fructus were extracted with 1000ml water in a boiling water bath for 2 h, and then add 60 g Rhei Rhizoma and boiled for 1 h. The supernatant was used for animal experiment. To extract Joweseunggitang, 60 g Rhei Rhizoma and 15 g Glycyrrhizae Radix were extracted with 1000 ml water in a boiling water bath for 3 h, and added Sodii Sulfas 30 g. The supernatant was used for animal experiment.

Assay of trypsin inhibition – The reaction mixture containing 0.4 ml of 1% casein, 0.1 ml of Seunggitangs was incubated at 37°C for 10 min, added 0.5 ml trypsin (unit)

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Table 1. The composition of Sunggitangs

Herbal medicine	Weight (g)		
	Daeseunggitang	Soseunggitang	Jowisunggitang
Rhei Rhizoma	15.0	15	15
Magnoliae Cortex	7.5	5.6	
Ponciri Fructus	7.5	5.6	
Sodii Sulfas	7.5		7.5
Glycyrrhizae Radix			3.8

and then incubated for 20 min. To stop the reaction, 1 ml of 5% trichloroacetic acid was added and centrifuged 3000 rpm for 10 min. Protein amount of the supernatant was measured according to the method of Lowry *et al.* (1951).

Minimum inhibitory concentration (MIC) – MICs of Seunggitangs were measured according to the method of Sherris (1989).

Assay of nitrite inhibition – RAW 264.7 cells (murine macrophage cell line) cultured in the Dulbeccos modified Eagles medium (DMEM) according to the previous method (Ryu *et al.*, 2000). Cells were dispended into 24-well plate at the concentration of 3×10^5 cells/well using DMEM without phenol red, and were stimulated by incubation in medium containing lipopolysacharide (1 mg/ml) and various concentrations of test materials for 2 hours. Then, cells were briefly centrifuged. The supernatant (0.15 ml) were incubated with an 0.15 ml of Griess reagent (0.2% naphthylethylene diamine in D.W : 2% sulfanilamide in 10% H_3PO_4 = 1:1) at room temperature for 10 min in 96 well microplate (light protected). The absorbance was measured by ELISA reader at 540 nm.

Assay of laxative activity – Male mice (ICR 20-25 g) were purchased from Samtaco Animal Co. (Korea), and maintained for one weeks before use and kept in metabolic cages for the experiments: Pellet foods (Hanlim Co., Korea) and water were freely available. All animal experiments carried out on 20-22°C and 50±10% humidity. Rhei Rhizoma (200 mg/kg) or its containing prescriptions (200 mg/kg as Rhei Rhizoma) were orally administered to 5 mice and D.W to 5 mice as a control. Fresh feces were compulsively obtained just before the administration of each sample and at 1, 2, 3, 4, 5 h after the administration of each sample. Their moisture content (%) was determined according to the following formula.

Moisture content (%) = [(fresh feces weight-dry feces weight)/fresh feces weight]×100

Large intestine transportation capacity – Male mice were fasted 12 hours before experiment, but water was freely available. And Rhei Rhizoma (200 mg/kg) or its containing prescriptions (200 mg/kg as Rhei Rhizoma) were orally administered to 3 mice and D.W to 3 mice as a control. 0.2 ml of 25% $BaSO_4$ 0.2 ml was administered orally 1 h after administration. The time of appearing feces containing 25% $BaSO_4$ was measured

Small intestine transportation capacity – Male mice were fasted 12 h before experiment, but water was freely available. And Rhei Rhizoma (200 mg/kg) or its containing polyprescriptions (200 mg/kg as Rhei Rhizoma) were orally administered to 3 mice and saline to 3 mice as a control. 0.2 ml of 25% $BaSO_4$ was administered orally 1 h after administration of each sample. Mice were expired 45 min after 25% $BaSO_4$ administration and then measured the 25% $BaSO_4$-migrated distance in the small intestine (Tamura *et al.*, 1972).

Results and Discussion

Seunggitangs (Soseunggitangs, Daeseunggitang, Jowiseunggitang) are representative purgatives in traditional Chinese medicine. The clinical applications of Seunggitangs are different. However, we could not find available data.

Dongwebogam decribes the pharmacological actions of ingredients of Seunggitang as follows: Rhei Rhizoma crashed the hardness of intestinal contents in patients with constipation, Sodii sulfas soften the hardness, Magnoliae Cortex pushes chronically accumulated intestinal contents, Ponciri fructus increases pushing chronically accumulated intestinal contents, and Glycyrrhizae fructus detoxifies the herb toxicity. Daeseunggitang, which is consisted of Rhei Rhizoma, Sodii sulfas, Magnoliae Cortex and Ponciri fructus, could be used as a purgative for patients with severe fever and chronic accumulated constipation. Soseunggitang, which is consisted of Rhei Rhizoma, Magnoliae Cortex and Ponciri fructus, could be used as a mild purgative for constipation. Jowiseunggitang, which is consisted of Rhei Rhizoma, Sodii sulfas and Glycyrrhizae Radix, could be used as a purgative for patients with febrile symptoms, fever, red urine and chronic accumulated constipation.

To evaluate the laxative activity of Seunggitangs, we administered these prescriptions to mice and measured the fecal moisture. Daeseunggitang contained the highest moisture

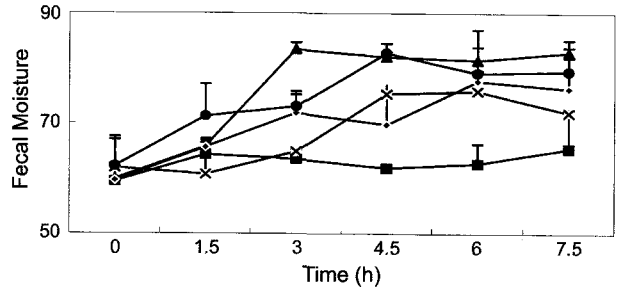

Fig. 1. Fecal Moisture of mice after orally administered Seunggitangs, Rhei Rhizoma.
–■– Control, –X– Rhei Rhizoma, –▲– Daeseunggitang, –◆– Soseunggitang –·– Joweseunggitang. Mice of the control group (closed square) were given same volume of d-water and the other groups were orally administered Rhei Rhizoma (the letter 'X'), Daeseunggitang (closed triangle), Soseunggitang (closed diamond), Joweseunggitang(closed circle).
Each sample administered 4 groups except control group, contains the same amount of Rhei Rhizoma, and the concentration of Rhei Rhizoma was 200 mg/kg.

in feces, followed by Joweseunggitang and Soseunggitang (Fig. 1). The moisture content of Soseunggitang was similar to that of Rhei Rhizoma alone. These results suggest that the purgative of Rhei Rhizoma is synergistically increased by Sodii Sulfas.

Small intestinal transportation of barium sulfate was increased by Seunggitangs. (Table 2). Daeseunggitang and Joweseunggitang were the most potent, followed by Soseunggitang and Rhei Rhizoma alone. Large intestinal transportation was also increased by Seunggitangs. Daeseunggitang and Joweseunggitang was the most potent, followed by Soseunggitang and Rhei Rhizoma alone. These results suggest that all Seunggitangs should be effective for constipation, but their purgative modes may be different.

Chronic constipation causes inflammation in colon. Therefore, we measured the inhibitory activitys of Seunggitangs on nitrite production of LPS-induced RAW 264.7 and trypsin (Table 3).

Soseunggitang exhibited the most potent inhibitory activity on nitrite production as well as on trypsin, followed by Jowiseunggitang and Daeseunggitang. Conspitation or diarrhea can cause the change of intestinal microflora. (Hopkins *et al.*, 2002 Sirakov *et al.*, 1981). Therefore, we measured minimum inhibitory concentrations of Seunggitangs for *E.coli* and *S. aureus*. Soseunggitang showed the most potent antibacterial activity for S. aureus, followed by Daeseunggitang and Jowiseunggitang. However, all Seunggitangs was not effective for E. coli. These results suggest that Magmoliae Cortex plays an important role in antibiotic activity.

The purgative components in Rhei Rhizoma are sennosides

Table 2. Intestinal transportation capacitiy of Seunggitangs

	Small intestine transportation (%)	Large intestine transportation (min)
Control	46±3.8	165±9.1
Rhei Rhizoma	50±5.5	145±5.5*
Daeseunggitang	65±8.5*	135±9.7*
Soseunggitang	57±8.6	147±9.0*
Joweseunggitang	64±6.5*	137±9.0*

Each sample except control group, contains the same amount of Rhei Rhizoma, and the concentration of Rhei Rhizoma was 200 mg/kg. Mice of control group were given same volume of d-water. Significance was determined by Students t-test.
*Significance was determined in a comparison to control group, $p<0.05$.

Table 3. Inhibitroy activities of Seunggitangs on trypsin, bacterial growth and nitrite production in LPS-induced RAW 246.7 cells

Concentration	IC_{50} (mg/ml)		MIC (mg/ml)
	Trypsin	NO production	
Daeseunggitang	2.66	1.042	4
Soseunggitang	2.19	0.281	2
Joweseunggitang	4.41	0.605	4

(Nonaka *et al.*, 1977; Oshino *et al.*,1974), which is activated by intestinal microflora (Kobashi *et al.*, 1980). Therefore, the purgative action of Rhei Rhizoma expresses in large intestine. However, the purgative activity of Sodii Sulfas expresses from small intestine. Therefore, we thought that Soseunggitang did not act in small intestine, but acted in large intestine. However, Daeseunggitang and Joweseunggitang acted from the small intestine to large intestine due to Sodii Sulfas and Rhei Rhizoma.

Based on these findings, Daeseunggitang can be used as a emergent purgative for patients with severe fever and constipation, Soseunggitang can be as a mild purgative for chronic constipation with inflammation and Jowiseunggitang can be as a potent purgative for patients for severe constipation and weak colitis.

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