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Purgative Activities of Whangryunhaedoktang and Chunghyuldan

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Abstract – The purgative activities of Whangryunhaedoktang (WT), Chunghyuldan (CD) and Rhei Rhizoma were measured to choose herbal formulae available for stroke patients suffering from constipation. When the laxative activity of Rhei Rhizoma and CD (the same dose as Rhei Rhizoma) compared, Rhei Rhizoma was more potent than CD. WT contained Gardeniae Fructus, which has been used as a laxative, as a ingredient. Nevertheless, WT did not show the purgative activity. WT and CD did not stimulate the transportation of small intestine. However, CD weakly stimulated the transportation of large intestine than Rhei Rhizoma. Accordingly, we believe that CD can be used as a useful purgative for stroke patients with constipation.

Key words – Whangryunhaedoktang, Chunghyuldan, purgative

Introduction

Whangryunhaedoktang (WT), which is consisted of Scutellariae Radix, Coptidis Rhizoma, Phellodendri Cortex and Gardeniae Fructus, is known to have the hypolipidemic activity (Haranaka *et al.*, 1986). Furthermore, this WT is known to increase cerebral blood flow (Yoshinaga *et al.*, 1992), to inhibit the blood pressure (Arakawa *et al.*, 1985; Hong *et al.*, 1982), and to exhibit antiinflammatory Suenaga *et al.*, 1991) and vasorelaxant activity (Higasa *et al.*, 1992) and so on. Daewhangwhangryunhaedoktang (DWT, Chunghyuldan), which is consisted of Rhei Rhizoma and ingredients of WT, showed potent inhibitory activity on HMG CoA reductase and pancreatic lipase in vitro, and significantly lowered blood cholesterol and triglyceride on hyperlipidemic animals.

Meanwhile, most arteriosclerotic patients suffer from constipation. It is thought to be a factor of stroke (Bae *et al.*, 1987). However, the purgative actions of WT and DWT frequently used for stroke patients were not studied.

Therefore, to care these arterosclerotic patients in Oriental Clinic, the purgative actions of WT and DWT were investigated in present study.

Materials and Methods

Materials – Coptidis Rhizoma, Phellodendri Cortex, Scutellariae Radix, Gardeniae Fructus and Rhei Rhizoma purchased from Kyung Dong Market (Seoul, Korea) and identified by Dr. Nam-Jae Kim, East-West Medical Research Institute, Kyung Hee Medical Center, Kyung Hee University. Voucher specimens (KHUVP01007-01011) were deposited at the Herbarium of College of Pharmacy, Kyung Hee University. The other chemicals were of analytical reagent grade.

CD A, CD B and CD C were consisted of 80% EtOH extract of 1 g, 2 g and 4 g Rhei Rhizoma in WT, respectively. The ingredients of WT were 80% EtOH extracts of Coptidis Rhizoma 4 g, Phellodendri Cortex 4 g, Scutellariae Radix 4 g, and Gardeniae Fructus 4 g (Kim *et al.*, 2002; Hong *et al.*, 1982).

Extraction of samples – One kilogram of each herbal medicine was extracted twice with 5 liter of 80% ethanol in boiling water for 2 h according to our previous method (Kim *et al.*, 2002). These extracts were filtered and evaporated in a rotary vacuum evaporator and then finally lyophilized with a freezing dryer. Dry weight yields (%) of extracts are shown in Table 1. To standardize the quality of these herbal medicines used in experiments, berberine, baicalin, geniposide, and sennoside A in WT, CD and Rhei Rhizoma were quantitatively assayed according to the previous methods (Oshima *et al.*, 1983; Hayakawa *et al.*, 1985; The Korean Pharmacopia, 1997). The main component contents of herbal medicine and formulae were shown in Table 1.

Assay of laxative activity – Assay of laxative activity was performed according to our previous method (Kim *et*

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Table 1. The extracted yield and component content from ingredients of Chunghyuldan and Whangryunhaedoktang

Herb	Scientific name	CD A	CDB	CD C	WT	Yield (%)	
						80% EtOH	Water
Coptidis Rhizoma	*Coptis japonica* MAKINO from Japan	4	4	4	4	15.8	11.8
Phellodendri Cortex	*Phellodendron amurense* RUPRECHT from China	4	4	4	4	10.9	9.3
Scutellariae Radix	*Scutellaria baicalensis* GEORGI from Young-am, Korea	4	4	4	4	32.0	34.3
Gardeniae Fructus	*Gardenia jasminoides* ELLIS from Young-am, Korea	4	4	4	4	28.3	18.3
Rhei Rhizoma	*Rheum palmatum* LINNE from China	1	2	4	0	35.3	18.3

Values indicate the major component content.

al., 2000). Male mice (ICR 20-25g) 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 or its containing prescriptions 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 1.5, 3.0, 4.5, 6.0 and 7.5 and 9.0 h after the administration of each sample. This experiment was repeated three times. 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 – Large intestine transportation capacity was performed according to the method of Tamura (1972). Male mice were fasted 12 hours before experiment, but water was freely available. And Rhei Rhizoma or its containing prescriptions 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. This experiment was repeated three times.

Small intestine transportation capacity – Small intestine transportation capacity was performed according to the method of Tamura (1972). Male mice were fasted 12 h before experiment, but water was freely available. And Rhei Rhizoma or its containing polyprescriptions 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. This experiment was repeated three times.

Results and Discussion

Whangryunhaedoktang (WT) is known to have the hypolipidemic activity (Haranaka *et al.*, 1986, to increase cerebral blood flow (Yoshinaga *et al.*, 1992), to inhibit the blood pressure (Arakawa *et al.*, 1985; Hong *et al.*, 1982) and to exhibit antiinflammatory (Suenaga *et al.*, 1991) and vasorelaxant activity (Higasa *et al.*, 1992) and so on. Chunghyuldan CD, which is consisted of Rhei Rhizoma and ingredients of WT, showed potent inhibitory activity on HMG CoA reductase and pancreatic lipase in vitro, and significantly lowered blood cholesterol and triglyceride on hyperlipidemic animals. These herbal formulae have been used for atherosclerotic patients or prevention of stroke. However, most these patients suffer from constipation. The purgative activity of WT and CD frequently used for stroke patients were not studied. Therefore, the purgative activities of WT, CD and Rhei Rhizoma were measured in order to guide herbal formulae available for stroke

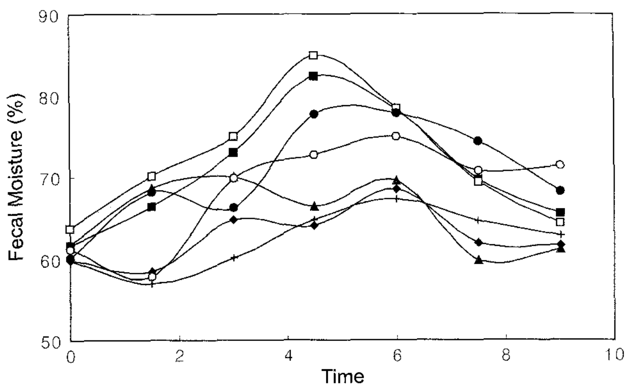

Fig. 1. The laxative effect of Whangryunhaedoktang and Chunghyuldan a ◆, Control; +, WT (1mg/kg); ▲, Chunghyuldan A (75 mg as Rhei Rhizoma); ○, Chunghyuldan B (150 mg as Rhei Rhizoma); ●, Chunghyuldan C (300 mg as Rhei Rhizoma); ■, Rhei Rhizoma (150 mg/kg); □, Rhei Rhizoma (300 mg/kg).

Table 2. The content of major components in 80% alcoholic extracts of Chunghyuldan and Whangryunhaedoktang

	Content (%)			
	Berberine	Baicalin	Geniposide	Sennoside A
Rhei Rhizoma.	–	–	–	0.76
Chunghyuldan A	5.07	5.74	4.99	0.06
Chunghyuldan B	5.07	5.74	4.99	0.11
Chunghyuldan C	3.97	4.50	3.91	0.22
Whangryunhaedoktang	5.59	6.32	5.49	0

Values are contents of major components in 80% alcoholic extracts.
Values in Parenthesis are contents of major components in water extracts.

patients suffering from constipation.

To evaluate the laxative activity of WT, CD and Rhei Rhizoma, we administered these herbal formulae (the same dose as a Rhei Rhizoma) to mice and measured the fecal moisture. Rhei Rhizoma alone group excreted the feces contained the higher moisture than CD (Fig. 1). Fecal moisture content of WT-treated group was lower than that of normal control group, even if WT contained Gardeniae Fructus, which is a laxative as a ingredient. These results suggest that the purgative of Rhei Rhizoma may be inhibited by ingredients of WT. Therefore, the purgative activity of CD was weaker than that of Rhei Rhizoma. Small intestinal transportation of barium sulfate was not affected by WT and CD like Rhei Rhizoma (Table 2). Large intestinal transportation was significantly increased by CD and Rhei Rhizoma. Rhei Rhizoma was more potent than CD, even if CD contained the same amount of Rhei Rhizoma. However, WT did not affect barium transportation in large intestine. These results suggest that its purgative activity of CD may be due to Rhei Rhizoma (not Gardeniae Fructus) but should be inhibited by its ingredients.

The purgative components in Rhei Rhizoma are sennosides (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 is expressed in large intestine. Both CD and WT are useful herbal formulae.

Based on these findings, we believe that CD can be used as a useful purgative for stroke patients with constipation.

Table 3. The transport capacity of Chunghyuldan, Whangryunhaedoktang and Rhei Rhizoma in small and large intestine

	Amount (mg/kg)	Small intestine transportation (%)	Large intestine transportation (min)
Control		68±3	171± 5.0
Rhei Rhizoma	150	–[a]	123±10.8
Rhei Rhizoma	300	67±4	108± 7.2
CD A	750	66±9	162± 7.5
CD B	1275	–	147± 6.1
CD C	1500	63±9	129±10.0
WT	1200	58±4	174± 7.2

[a]not determined.

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