

## 仙方活命飲의 抗菌效能 및 成分에 關한 研究

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### ABSTRACT

#### Studies on the Antibacterial Activity and Active Constituents of Sonbanghwalmyeongum

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藥效 및 安定성이 立證된 韓藥으로부터 새로운 抗菌劑를 導出하고자, 臨床에서 清熱作用이 있거나 炎症性 疾患과 박테리아의 感染으로 비롯된 疾患에 자주 쓰이는 22個의 處方에 對해 paper disk 法을 使用하여 抗菌 效能을 檢索하였다. 試料는 韓藥의 服用 方法을 考慮하여 물로 抽出하였으며, 使用 菌柱로는 그람 陽性菌인 葡萄狀球菌과 枯草菌 그리고 그람 陰性菌인 大腸菌과 綠膿菌을 使用하였고, 對照物質로는 tetracycline 을 使用하여 常法에 依해 實驗하였다. 22個의 處方 가운데 白頭翁湯, 黃連解毒湯, 增黃連黃連解毒湯, 瀉心湯, 龍膽瀉肝湯, 仙方活命飲 等の 處方이 卓越한 抗菌 活性을 보였다.

이 가운데 本 研究에서는 湯劑의 構成 藥材가 다른 處方들에 비해 比較의 多樣한 仙方活命飲에 對해 活性 成分의 糾明 및 構成 藥材間의 相互作用을 밝히고자 하였다. 仙方活命飲 5 kg 을 메탄올 (MeOH) 로 抽出한 뒤 優秀한 抗菌 活性을 보인 에칠아세테이트 (EtOAc) 分割에 對하여 silica gel 및 Sephadex LH-20 column chromatography 를 反復하여 stilbene 系列의 化合物인 Rhapontigenin (Compound 1) 과 Rhaponticin (Compound 2) 을 얻었다.

*S. aureus* SG 511 에 對해 Rhapontigenin 은 50 mg/ml 以上 濃度에서 抗菌 效果를 나타내었고, Rhaponticin 은 200 mg/ml 濃度에서 微弱하게 有效한 抗菌 效果를 나타내었으며, *B. subtilis* ATCC 6633 에 對해 Rhapontigenin 은 50 mg/ml 以上 濃度에서 抗菌 效果를 나타내었고, Rhaponticin 은 200 mg/ml 濃度에서 優秀한 抗菌 效果를 나타내었으며, 100 mg/ml 濃度에서 微弱하게 有效한 抗菌 效果를 나타내었다. 또한 *E. coli* 055 에 對해서는 Rhapontigenin과 Rhaponticin 모두 200 mg/ml 濃度에서 微

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弱하게 有效한 抗菌 效果를 나타내었다.

以上の 結果로 보아 仙方活命飲의 抗菌 效能은 君藥인 大黃의 成分 中の 하나인 stilbene 系列의 化合物인 Rhapontigenin 과 Rhaponticin 의 作用에 依한 것이며, 이는 韓醫學 方劑 原理인 君臣佐使 理論에서 君藥이 主症에 主로 作用하는 藥物이라는 것을 밝혀주는 것이라고 思料된다.

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Key Word : 抗菌活性, 韓藥, 仙方活命飲, 君臣佐使, rhapontigenin, rhaponticin, stilbene誘導體.  
(antibacterial activity, the oriental herbal medicine, Sonbanghwalmyeongum, 4 regular parts of oriental prescriptions, stilbene derivative.)

## I . Introduction

The Oriental countries including Korea, China and Japan have been using oriental herbal medicines to cure many diseases since old times. Because of its long history and experiences in the usage of oriental herbal medicines, the development of new drugs from oriental herbal medicines may avoid side effects or toxicities of synthetic drugs. Therefore, oriental herbal medicines have been regarded as a gold mine for the development of a new medicine. Although, many studies on antibacterial activities of extracts or components of plants growing or cultivated in Korea have been reported,<sup>1-3)</sup> no report has been made so far on the antibacterial activities and active constituents of oriental prescriptions which have been used clinically to clear away pathogenic heat (清熱) or to treat inflammatory lesions and bacterial infections in Korea.

In order to develop new antibacterial agents from oriental herbal medicines, antibacterial activities of water extracts from

22 kinds of oriental herbal medicines were screened in vitro by the paper disk assay method.<sup>4-5)</sup> Among them, water extracts of Baektuongtang, Hwangyonhaedoktang, Hwangyonhaedoktang plus hwangyon (ten times dosed hwangyon), Sasimtang, Yongdamsagantang showed remarkably potent antibacterial activity. Although Sonbanghwalmyeongum showed weaker antibacterial activity than above mentioned prescriptions, it was chosen on account of the diversity of its prescription.

In order to identify both antibacterial components and interactions of their constituents of Sonbanghwalmyeongum, fractionations and activity-guided purification procedures were repeatedly carried out by silica gel and Sephadex LH-20 column chromatography. As a result, two active stilbene derivatives, rhapontigenin (compound 1) and rhaponticin (compound 2) were obtained. In this work, we report the result of screening as to oriental herbal medicines for antibacterial activities and the isolation of active constituents of Sonbanghwalmyeongum.

## II. Materials and Methods

### General Experimental Procedures

Melting points were determined on a Thomas-Hoover capillary melting point apparatus (uncorrected). UV spectra were taken by a Pharmacia Biotech Ultrospec 2000 UV/Visible Spectrometer. IR spectra were recorded on a Midac High Resolution FT-IR Spectrometer using potassium bromide pellets.  $^1\text{H}$ -NMR spectra were recorded on a Varian Unity 300 (300 MHz) spectrometer using TMS as internal standard.  $^{13}\text{C}$ -NMR spectra were recorded on a Varian Unity 300 (75.5 MHz) spectrometer. EIMS were determined on a HP 5890 GC/HP 5972 mass selective detector at 70 eV. HPLC was performed by Waters pump (model 501) with UV detector ( $\lambda$  254 nm, Waters model 441) using a LiChrosorb RP-18 (4 mm i.d. x 250 mm, Merck) column. Cellulose TLC was carried out by precoated cellulose F TLC plates (Merck, art. 5718).

### Oriental Herbal Medicines

Oriental herbal medicines were purchased at Kyoungdong market in Korea and authenticated from the division of herbology in Kyung-Hee University.

The constitutional drugs of Sonbhanghwalmyeongum<sup>6)</sup> : Rhei Rhizoma 20 g, Lonicerae Flos 12 g, Angelicae gigantis Radix, Gleditsiae Spina and Aurantii nobilis Pericarpium each 6 g, Olibanum, Fritillariae thunbergii Bulbus, Trichosanthis Radix, Paeoniae Radix rubra, Glycyrrhizae Radix, Manitis Squama and Angelicae dahuricae Radix each 4 g, Saposh-

nikoviae Radix 2.8 g, Myrrha 2 g. Voucher specimens have been deposited in the laboratory of Korea Institute of Science & Technology.

### Preparation of Sample Extracts for the Test of Antibacterial Activity

Since oriental herbal medicines have been clinically used as water extracts, each sample was extracted to the amount of 300 ml by boiling down both 3 packages of oriental herbal medicines and 900 ml of water for 2 hours, in an open vessel. After the hot extract was filtered and lyophilized, the resulting extract was tested. 200 mg of samples were dissolved in water respectively and diluted to appropriate concentrations (200 mg/ml, 100 mg/ml, 50 mg/ml) and then filtered with a microfilter (Stervix 0.22  $\mu\text{m}$ ) prior to testing.

### Test Organisms

Two Gram positive bacteria, *Staphylococcus aureus* SG 511, *Bacillus subtilis* ATCC 6633, and two Gram negative bacteria, *Escherichia coli* 055, *Pseudomonas aeruginosa* 9027, were used as test organisms.

### Antibacterial Activity Test

Each strain was cultured in 10 ml of Fleisch Extract Broth (Beef Extract 10 g, Bacto Peptone 10 g, NaCl 3 g,  $\text{Na}_2\text{HPO}_4 \cdot 12 \text{H}_2\text{O}$  2 g/1 l distilled water) at 37 °C for 18 hours. After cultivating for 18 hours, the turbidity of bacterial suspensions was adjusted with the same sterile broth as Fleisch Extract Broth

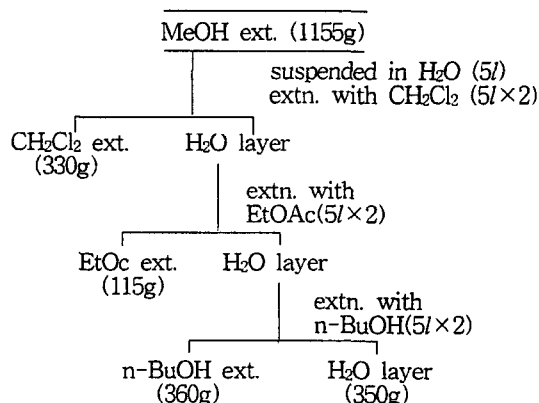
from 0.02 to 0.03 optical density (OD) at 540 nm and then used for the tests. For the paper disk assay method, 2 ml of the bacterial suspensions was poured uniformly into the plate (size 245 mm x 245 mm x 20 mm, Nunc) made of 88 ml of Mueller Hinton agar (Beef, Infusion from 300 g, Bacto Casamino Acids, Technical 17.5g, Starch 1.5g, Bacto Agar 17g) as media. The paper disks (6 mm in diameter, Difco) containing 2 mg, 1 mg and 0.5 mg of samples were carefully placed on the plate and were allowed to diffuse for 1 hour at 4 °C in a refrigerator. Further cultivation was followed at 37 °C for 18 hours and the clear inhibition zone was observed with the naked eyes.

### Extraction and Isolation of Active Constituents from Sonbhangwalmyongum

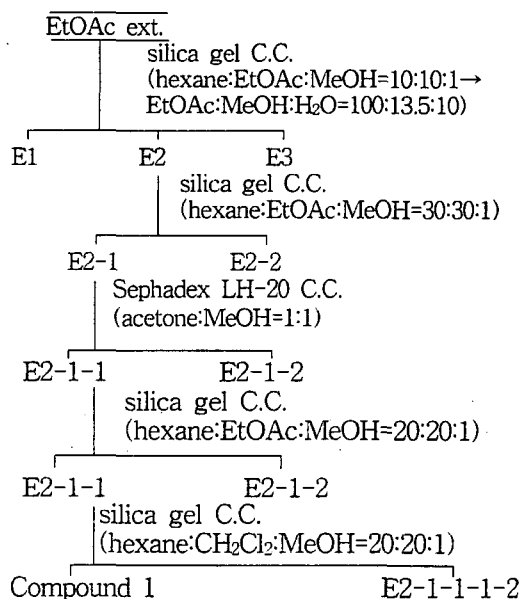
Sonbhangwalmyongum (5.0 kg) was percolated three times with MeOH at the room temperature to afford 1,155 g of a dark residue on removal of solvent under reduced pressure. The methanol extract was suspended in water, and then partitioned in turn with dichloromethane, ethyl acetate, and butanol. The combined EtOAc extract was evaporated under reduced pressure to yield 115 g of residue. This residue was divided into three subfractions (E1, E2 and E3) by silica gel column chromatography using gradient system from hexane:EtOAc:MeOH (10:10:1) to EtOAc:MeOH:H<sub>2</sub>O (100:13.5:10). The active subfraction E2 was further purified by silica gel column chromatography with hexane:EtOAc:MeOH (30:30:1) system to afford two subfractions (E2-1 and E2-2).

Repeated silica gel and Sephadex LH-20

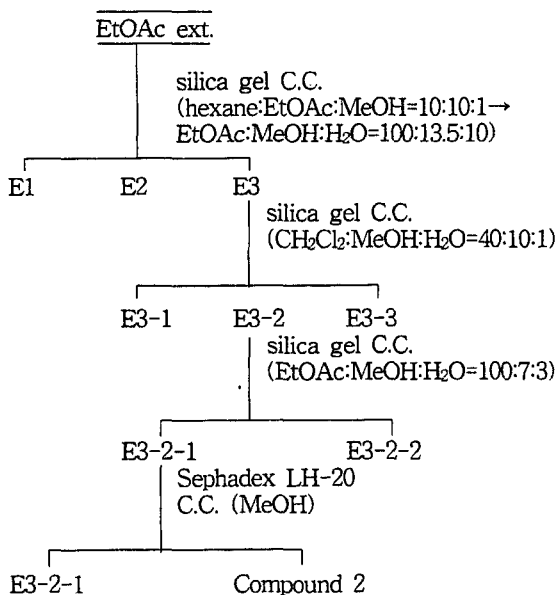
column chromatography for the active subfraction E2-1 afforded 60 mg of compound 1 as brownish crystal. The active subfraction E3 was also further purified by column chromatography similar to above mentioned manner to yield 50 mg of compound 2 as a pale yellowish amorphous powder.(Scheme I, II, III)



**Scheme I.** Extraction and Fractionation of Sonbhangwalmyongum



**Scheme II.** Isolation of Compound 1 from EtOAc ext. of Sonbhangwalmyongum(C.C.= column chromatography)



Schme III. Isolation of Compound 2 from EtOAc ext. of Sonbhanghwalmyeongum(C.C.=column chromatography)

Rhapontigenin (1) : Brownish crystal ; m.p. 195~197 °C ; UV  $\lambda_{\max}$  (MeOH) nm : 222, 302, 324 ; IR  $\nu_{\max}$  (KBr)  $\text{cm}^{-1}$  : 3284 (OH), 1594, 1512 (aromatic C=C) ; GC/MS (m/z) : 258 ( $M^+$ , 100), 225, 197, 169, 141, 129, 115 ;  $^1\text{H-NMR}$  (300 MHz,  $\text{CD}_3\text{OD}$ ) : 3.80 (3H, s,  $-\text{OCH}_3$ ), 6.14 (1H, t,  $J=2.1$  Hz, H-4), 6.41 (2H, d,  $J=2.1$  Hz, H-2, H-6), 6.74, 6.86 (each 1H, d,  $J=15.9$  Hz, olefinic-H), 6.83 (1H, d,  $J=8.4$  Hz, H-5'), 6.88 (1H, dd,  $J=1.8, 8.4$  Hz, H-6'), 6.96 (1H, d,  $J=1.8$  Hz, H-2') ;  $^{13}\text{C-NMR}$  (75.5 MHz,  $\text{CD}_3\text{OD}$ ) : 141.4 (C-1), 106.2 (C-2), 159.9 (C-3), 103.1 (C-4), 159.9 (C-5), 106.2 (C-6), 132.5 (C-1'), 113.9 (C-2'), 148.0 (C-3'), 149.3 (C-4'), 113.0 (C-5'), 120.3 (C-6'), 128.1 ( $\alpha$ ), 129.7 ( $\beta$ ), 56.7 ( $-\text{OCH}_3$ )

Rhaponticin (2) : Pale yellowish powder ; m.p. 246~249 °C ; UV  $\lambda_{\max}$  (MeOH) nm :

220, 302, 324 ; IR  $\nu_{\max}$  (KBr)  $\text{cm}^{-1}$  : 3348 (OH), 1616, 1588, 1514 (aromatic C=C), 1072 (glycosidic C-O) ;  $^1\text{H-NMR}$  (300 MHz,  $\text{DMSO}-d_6$ ) : 3.15~3.85 (6H, m, sugar-H), 3.78 (3H, s,  $-\text{OCH}_3$ ), 4.80 (1H, d,  $J=6.9$  Hz, anomeric-H), 6.34 (1H, t,  $J=2.1$  Hz, H-4), 6.56, 6.70 (each 1H, brs., H-2, H-6), 6.81, 6.96 (each 1H, d,  $J=16.0$  Hz, olefinic-H), 6.88 (1H, d,  $J=8.4$  Hz, H-5'), 6.94 (1H, dd,  $J=8.3, 1.9$  Hz, H-6'), 6.99 (1H, d,  $J=1.8$  Hz, H-2'), 4.60, 4.99, 5.05, 5.25 (sugar  $-\text{OH}\times 4$ ,  $\text{D}_2\text{O}$  exchange), 8.96, 9.42 (aromatic ring  $-\text{OH}\times 2$ ,  $\text{D}_2\text{O}$  exchange) ;  $^{13}\text{C-NMR}$  (75.5 MHz,  $\text{DMSO}-d_6 + \text{D}_2\text{O}$ ) : 139.8 (C-1), 105.6 (C-2), 159.4 (C-3), 103.4 (C-4), 158.7 (C-5), 107.6 (C-6), 130.5 (C-1'), 113.2 (C-2'), 146.9 (C-3'), 148.3 (C-4'), 112.7 (C-5'), 119.4 (C-6'), 126.6 ( $\alpha$ ), 129.2 ( $\beta$ ), 56.2 ( $-\text{OCH}_3$ ) 101.0 (C-1''), 73.7 (C-2''), 77.4 (C-3''), 70.3 (C-4''), 76.9 (C-5''), 61.2 (C-6'')

### III. Results and Discussion

#### The Antibacterial Activities as to 22 Kinds of Oriental Prescriptions

The antibacterial activities as to 22 kinds of oriental prescriptions, most of which are commonly used to treat bacterial infections in Korea, were screened by the paper disk assay method.

The antibacterial activities are represented on the basis of the following criterion : an inhibitory zone below 8.0 mm in diameter is negative in antibacterial activity and that over 8.0 mm is positive.<sup>7)</sup> The latter is further classified by three grades based on their activities. Table I summarized the results of

antibacterial activities as to 22 kinds of oriental prescriptions.(Table I)

Among these extracts, Baektuongtang, Hwangyonhaedoktang, Hwangyonhaedoktang plus hwangyon (ten times dosed hwangyon), Sasintang and Yongdamsagantang showed potent antibacterial activities.

It is of interest to compare the antibacterial activity of Hwangyonhaedoktang plus hwangyon (ten times dosed hwangyon) with that of Hwangyonhaedoktang. Both of them consist of Coptidis Rhizoma, Gardeniae Fructus, Phellodendri Cortex and Scutellariae Radix.<sup>8)</sup>

But the amount of Coptidis Rhizoma of Hwangyonhaedoktang plus hwangyon is ten times as much dosed as that of Hwangyonhaedoktang. Therefore, it is suggested that the constituents of Coptidis Rhizoma of Hwangyonhaedoktang play a major role in the improvement of antibacterial activity. Besides, Sonbanghwalmyeongum including Rhei Rhizoma as 'a monarch drug' (君藥) showed antibacterial activity while Soungtang which consists of the same prescription as Sonbanghwalmyeongum except Rhei Rhizoma showed no activity. Based on these results, it is suggested that the

Table I. Antibacterial Activities of Extracts of Various Herbal Medicines

Herbal Medicines	Strains		Antibacterial Activities											
	Concentrations (mg/ml) (a)		S. aureus SG 511			B.subtilis ATCC 6633			E.coli 055			P.aeruginosa 9027		
	200	100	50	200	100	50	200	100	50	200	100	50		
Baektuongtang	++	-	-	-	-	-	-	-	-	-	-	-		
Chongsoikkitang	-	-	-	-	-	-	-	-	-	-	-	-		
Chongyolsasuptang	-	-	-	-	-	-	-	-	-	-	-	-		
Haedongnaetaksan	-	-	-	-	-	-	-	-	-	-	-	-		
Hwalhyolgupungtang	-	-	-	-	-	-	-	-	-	-	-	-		
Hwangyonhaedoktang	++	-	-	-	-	-	-	-	-	-	-	-		
Hwangyonhaedoktang plus hwangbaek(l)	+	-	-	-	-	-	-	-	-	-	-	-		
Hwangyonhaedoktang plus hwangyon(c)	++++	+++	+++	+	+	-	-	-	-	-	-	-		
Kamihwangyonhaedoktang	-	-	-	-	-	-	-	-	-	-	-	-		
Ojoksan	-	-	-	-	-	-	-	-	-	-	-	-		
Oyaksungisan	-	-	-	-	-	-	-	-	-	-	-	-		
Samyoyongantang	-	-	-	-	-	-	-	-	-	-	-	-		
Sasintang	++	+	-	+++	++	-	-	-	-	-	-	-		
Sonbanghwalmyeongum	+	-	-	-	-	-	-	-	-	-	-	-		
Sopunghwalhyoltang	-	-	-	-	-	-	-	-	-	-	-	-		
Soungtang	-	-	-	-	-	-	-	-	-	-	-	-		
Taebangpungtang	-	-	-	-	-	-	-	-	-	-	-	-		
Taeganghwaltang	-	-	-	-	-	-	-	-	-	-	-	-		
Tanglisodogum	-	-	-	-	-	-	-	-	-	-	-	-		
Tojoksan	-	-	-	-	-	-	-	-	-	-	-	-		
Yongdamsagantang	++	-	-	-	-	-	-	-	-	-	-	-		
Youngsonjetongum	-	-	-	-	-	-	-	-	-	-	-	-		

(a) The antibacterial activity is represented as follows : -, no inhibitory zone was formed; +, inhibitory zone was formed within 8mm; ++, 9~12mm; +++, 13~16mm; ++++ more than 17 mm in diameter.

(b) Hwangyonhaedoktang(ten times dosed Hwangbaek)

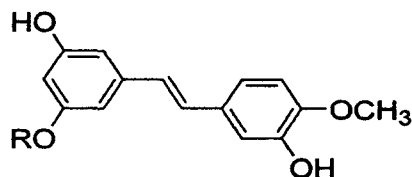
(c) Hwangyonhaedoktang(ten times dosed Hwangyon)

constituent of Rhei Rhizoma is essential to the antibacterial activity of Sonbhangwalmyongum.

## The Antibacterial Constituents of Sonbhangwalmyongum

In order to identify the antibacterial components and the interactions of their constituents of Sonbhangwalmyongum, fractionations and activity-guided purification procedures were repeatedly carried out by silica gel and Sephadex LH-20 column chromatography to afford two active compounds (1 and 2).

Compound 1 was recognized as one of the stilbene derivatives from characteristic absorption bands of the UV<sup>9-10</sup> and IR spectrum. The GC/MS spectrum showed a molecular ion peak at  $m/z$  258. The <sup>1</sup>H-NMR spectrum of compound 1 showed peaks at both  $\delta$  6.14 (1H, t,  $J=2.1$  Hz) and  $\delta$  6.41 (2H, d,  $J=2.1$  Hz) due to H-4, H-2 and H-6 of the trisubstituted aromatic ring and showed peaks at  $\delta$  6.83 (1H, d,  $H=8.4$  Hz, H-5'),  $\delta$  6.88 (1H, dd,  $J=1.8, 8.4$  Hz, H-6') and  $\delta$  6.96 (1H,  $J=1.8$  Hz, H-2') due to the 3H ABX system of the 1-phenyl 3', 4'-disubstituted ring system. The peaks at both  $\delta$  6.74 (1H, d,  $J=15.9$  Hz) and  $\delta$  6.86 (1H, d,  $J=15.9$  Hz) resulted from olefinic protons and turned out to be *trans* conformation from the coupling constants.<sup>11)</sup> In addition, the -OCH<sub>3</sub> peak at C-4' was observed at  $\delta$  3.80. When these <sup>1</sup>H-NMR and <sup>13</sup>C-NMR data (see experiment) were compared with those reported in the literature,<sup>12-13)</sup> compound 1 was identified as 3, 3', 5-trihydroxy-4'-methoxystilbene, rhapontigenin. (Fig. 1)



Compound 1 R=H

Compound 2 R=β-D-Glucose

Fig. 1. Structures of Compound 1 and 2

Compound 2 showed very similar absorption bands of UV spectrum to those of compound 1. The IR spectrum of compound 2 showed characteristic absorption bands due to hydroxyl groups ( $3348\text{ cm}^{-1}$ ), aromatic double bonds ( $1616, 1588$  and  $1514\text{ cm}^{-1}$ ) and glycosidic C-O bond ( $1072\text{ cm}^{-1}$ ), respectively. The <sup>1</sup>H-NMR spectrum of compound 2 showed peaks at  $\delta$  6.34 (1H, t,  $J=2.1$  Hz),  $\delta$  6.56 and  $\delta$  6.70 (each 1H, brs.) due to H-4, H-2 and H-6 of the trisubstituted aromatic ring and showed peaks at  $\delta$  6.88 (1H, d,  $J=8.4$  Hz, H-5'),  $\delta$  6.94 (1H, dd,  $J=1.9, 8.3$  Hz, H-6') and  $\delta$  6.99 (1H, d,  $J=1.8$  Hz, H-2') due to the 3H ABX system of the 1-phenyl 3', 4'-disubstituted ring system. The peaks at both  $\delta$  6.81 (1H, d,  $J=16.0$  Hz) and  $\delta$  6.96 (1H, d,  $J=16.0$  Hz) originated from an olefinic protons and turned out to be *trans* conformation from the coupling constants. Also, the -OCH<sub>3</sub> peak at C-4' was observed at  $\delta$  3.78 (3H, s, -OCH<sub>3</sub>). It is strongly suggested that Compound 2 is stilbene glycoside from the peaks at both  $\delta$  3.15~ $\delta$  3.85 (6H, m) due to sugar protons and  $\delta$  4.80 (1H, d,  $J=6.9$  Hz) originated from an anomeric proton. The sugar was identified as D-glucose by co-TLC after acid hydrolysis of compound 2. The

configuration of D-glucose proved to be  $\beta$ -form from the coupling constant. When these  $^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  data (see experiment) were compared with those reported in the literature,<sup>14-15)</sup> compound 2 was identified as 3, 3', 5-trihydroxy-4'-methoxy stilbene-3-O- $\beta$ -D-glucoside, rhaponticin.(Fig. 1)

Against *S. aureus* SG 511, rhapontigenin showed antibacterial activity at the concentration of 50 mg/ml and rhaponticin showed weak antibacterial activity at the concentration of 200 mg/ml. Rhapontigenin and rhaponticin showed antibacterial activities against *B. subtilis* ATCC 6633 at the concentration of 50 mg/ml and 200 mg/ml, respectively. Rhaponticin also showed weak antibacterial activity against *B. subtilis* ATCC 6633 at the concentration of 100 mg/ml. In addition, rhapontigenin and rhaponticin showed weak antibacterial activities against *E. coli* 055 at the concentration of 200

mg/ml.(Table II)

### The Investigation of the Literature on Carbuncle (癰疽) and Sonbhangwalmyeongum (仙方活命飲)

Carbuncle indicates a sort of surgical disease over the body surface that is brought about because of severe pathogenic heat-toxin (熱毒), which is produced by the stagnation (壅滯) of either the nutrient and superficial defensive system (營衛) or the vital energy and blood (氣血) in the channel system (經脈).

Etiological factors of carbuncle are either pathogenic heat-toxin or heat-toxin by evils attacking the body in general debility (虛邪) or heart-fire (心火) and so on. Pathogenic heat-toxin results either from such improper diet intake (飲食不節) as overeating rich fatty diet (膏粱厚味), fishes and salt, or from long-time administration of pill and powder (丸

Table II. Antibacterial Activities of Compound 1 and 2 from Sonbhangwalmyeongum

Strains, Concentrations (mg/ml) Fractions	Staphylococcus aureus SG 511				Bacillus subtilis ATCC 6633				Escherichia coli 05E				Pseudomonas aeruginosa 9027			
	200	100	50	25	200	100	50	25	200	100	50	25	200	100	50	25
Compound 1	++++ (17)	+++ (13)	++ (10)	-	+++ (15)	+++ (14)	++ (11)	-	±	-	-	-	-	-	-	-
Compound 2	±	-	-	-	++ (10)	±	-	-	±	-	-	-	-	-	-	-
Tetracycline	( 28 )				( 30 )				( 26 )				( 11 )			

\* The antibacterial activity is represented as follows : -, no inhibitory zone was formed ; ±, the inhibitory zone but is not clear ; +, inhibitory zone was formed within 8mm ; ++, 9-12mm ; 13-16mm ; +++++, more than 17mm in diameter.

\* ( ) : The diameter of inhibitory zone (size : mm)



散劑) made of melted or sublimated minerals and stones (丹石藥) which contain dry and hot nature (燥熱之性). Heat-toxin by evils attacking the body in general debility is produced either by an unpredictable temper (喜怒不時) or by inharmonious cold and heat (寒暑不調) or by uncontrolled liking and desire (嗜慾無節).<sup>16-18)</sup>

In the western medicine, carbuncle is known by the name of acute suppurative inflammatory diseases produced between the skin and muscle by bacterial infection, which is applicated to subcutaneous abscess, acute suppurative lymphnoditis and so forth.

Carbuncle is divided into the positive (Yang) and the negative (Yin) syndrome (陽症 陰症) by its nature. The erosion of muscles, ulceration and suppuration progress rapidly as benignity in the positive syndrome, where are fever, pain, red color and contraction or eminence of core of root. After suppuration is formed, neoformative vital energy and blood (新生氣血) replace the suppurative lesion, which turns red again in the end after ulceration. In negative syndrome, suppuration makes a slow progress and spreads as miliary pus head. Deep-rooted carbuncle (陰疽) is lustreless, dark purple and hard without edema, fever and pain. When skin ulceration is formed and the thin pus comes out, it sometimes smells nasty.<sup>19)</sup>

Sonbangwhalmyongum has been used to treat carbuncle which is a kind of inflammatory diseases since it was first recorded in 'The Complete Book of Effective Prescriptions for Wemen' (婦人良方大全)<sup>20)</sup> by Chen (陳自明) in Song dynasty (宋代). It was recorded as a

nice herbal medicine in relieving swelling to stop pain (消腫止痛) as well as in either relieving infectious swelling before formative stage of suppuration (未成者即散) or ulcerating all kinds of pyogenic infections after formative stage of suppuration (已成者即潰).

Although Sonbangwhalmyongum has been changed a little in the drug of formulating a prescription, it has been used for a long time by such various masters as Hur (許浚) writing 'Treasured Mirror of Oriental Medicine' (東醫寶鑑)<sup>6)</sup> since Rhei Rhizoma (大黃) was added in 'Elementary Course for Medicine' (醫學入門)<sup>21)</sup> written by Li (李梴).

The principle of composition of oriental herbal prescriptions is based on the theory of four regular parts, namely, 'monarch, minister, assistant and guide' (君臣佐使). The monarch drug works directly on main symptoms as main drug in a prescription. The minister drug assists and makes the effect of monarch drug stronger. The assistant drug has restrainable effect against the monarch drug and has the action to release accessory symptoms by helping monarch drug. The guide drug becomes medicinal guide (引經藥) and indicates attendant drug among a prescription.<sup>22)</sup>

The monarch drugs of Sonbangwhalmyongum are Rhei Rhizoma and Lonicerae Flos. The minister drugs are Angelicae gigantis Radix, Aurantii nobilis Pericarpium, Fritillariae thunbergii Bulbus, Trichosanthis Radix, Paeoniae Radix rubra, Glycyrrhizae Radix, Angelicae dahuricae Radix and Saposhnikoviae Radix. The assistant drugs are Olibanum and Myrrha. The guide drugs are Gleditsiae Spina and Manitis Squama.<sup>23)</sup>

The herbal effects on constitutional drugs of Sonbhangwalmyongum are as follows ;

Rhei Rhizoma purges pathogenic fire to cool the pathogenic heat from the blood (瀉火涼血) and clears away pathogenic heat and toxicant (清熱解毒). Lonicerae Flos becomes the holy drug (聖藥) of carbuncle by clearing away heat and removing toxic materials (散熱解毒). Trichosanthis Radix eliminates phlegm to lower the evil fire (清痰降火). Angelicae dahuricae Radix removes dampness and disperses pathogenic wind (除濕祛風) and also promotes pus discharge to reduce swelling (排膿消腫). Angelicae gigantis Radix regulates the function of the negative principle in nature to activate blood circulation (和陰而活血). Paeoniae Radix rubra activates blood circulation to dissipate blood stasis (活血散瘀) and also relieves swelling and stop pain. Aurantii nobilis Pericarpium dries the wetness evil and promotes vital energy circulation (燥濕行氣). Saposhnikoviae Radix dispels the pathogenic wind (消散風邪), in addition to both purging the pathogenic fire of the lung and relieving the vital energy of the depressed liver(瀉肺疏肝). Fritillariae thunbergii Bulbus reduces phlegm to resolve hard masses(利痰散結). Glycyrrhizae Radix coordinates toxic materials and regulates the stomach(化毒和中). Olibanum regulates the flow of the vital energy(調氣) and expels the toxin by reinforcing the vital energy and blood and protecting the function of heart(托裏護心). Myrrha reduces swelling to arrest pain by dissipating blood stasis. Manitis Squama leads the drug to the affected sites to relieve infectious swelling or masses(善走能散). Since Gleditsiae Spina penetrates the channels and collaterals(貫穿經絡) to guide various drugs quickly and directly to the affected lesions, it festers

carbuncle to break hard masses(潰癰破堅).<sup>23)</sup>

Therefore, the nature and taste of Sonbhangwalmyongum has a tendency to be slightly cold and nontoxic, bitter and sweet. The orders of high frequency in the use of attributive channel (歸經) are the Liver, the Spleen, the Stomach, the Lung and the Heart Channel. The effect on a prescription of Sonbhangwalmyongum is to activate of blood circulation to alleviate pain as well as both to reduce swelling to fester hard masses (消腫潰堅) and to drain off pus (排膿), by clearing away pathogenic heat and toxicant.

Consequently, this prescription can be applied to the carbuncle of the positive syndrome which is produced by the pathogenic heat-toxin at the primary stage of skin and external diseases and pyogenic infections (瘡瘍腫毒) when the condition of body is sturdy.

Based on the result so far achieved, it is suggested that the stilbene derivatives, rhapontigenin and rhaponticin, were responsible for the antibacterial effect of Sonbhangwalmyongum. And it seems that this could verify that the monarch drug works mainly on curing main symptoms in the theory of four regular parts of oriental prescriptions, namely, monarch, minister, assistant and guide.

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