

# Effects of Rehmanniae Radix and Radix Aconiti Water Extracts on Blood Pressure in Hypertensive Rats

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## 속지황, 부자 전탕액이 고혈압 백서의 혈압에 미치는 영향

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### 국문초록

한의학에 있어서 음양의 조절은 매우 중요하다. 속지황은 음허를 치료하는 주약이며, 부자는 양허를 치료하는 주약이다. 한의학에서 신성고혈압의 발생은 음허와 관련이 있다고 하였다. 본 연구는 실험적 신성고혈압과 자연발증고혈압 백서에 속지황과 부자 전탕액을 투여 후 혈압의 변동과 혈장 renin 활성도, aldosterone 및 심방이노호르몬 (atrial natriuretic hormone)의 변동을 관찰하였다. 속지황 투여 후 실험적 신성고혈압 백서의 혈압은 감소하였다. 부자 전탕액 투여 후 자연발증고혈압 백서의 혈압 상승이 억제되었다. 속지황 및 부자 전탕액 투여 후 자연발증고혈압 백서의 혈장 renin 활성도는 감소하였다. 부자 전탕액 투여 후 신성고혈압 백서의 혈장 ANP 농도는 감소하였다. 부자 전탕액의 혈압강하 작용은 ANP 및 aldosterone 농도의 변동과 관련이 있다고 사료된다.

중심단어 : 고혈압, 속지황, 부자, Renin, Aldosterone, ANP

### Introduction

Rehmanniae Radix is the root of *Rehmannia glutinosa* LIBOSCH. var. *purpurea* MAKINO (Takaki et al., 1985). There are three types of *Rehmanniae Radix*

according to the methods of preparation namely, Sheng-Di-Huang, Kan-Di-Huang, Shou-Di-Huang (Takaki et al., 1985). Shou-Di-Huang is the steam-dried root of *Rehmannia glutinosa*, *Rehmanniae Radix* and it has long been used as a tonic in oriental medicine for many years (Hsu et al., 1986). It is made by taking juicy roots, washing them in millet wine, steaming on a willow frame in a porcelain vessel, drying, and resteamng and redrying nine times (WHO, 1969) Yun (Yun et al., 1981) has reported that an extract of *Rehmannia glutinosa* inhibits angiotensin converting

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enzyme. In this study we investigated the effects of steamed *Rehmanniae Radix* (Shou-Di-Huang) and *Radix Aconiti* water extract on blood pressure and endocrine function in hypertensive rats.

## Materials and Methods

### *Reagents*

600 g of *Rehmanniae Radix* and 75 g of *Radix Aconiti* sample were extracted with 1500 ml of distilled water for 120 minutes at 100 °C. The water extracts were centrifuged and filtrated with filter paper. After filtration it was dried by a rotary vacuum evaporator at 60 °C

### *Animals*

A total of 45 male Sprague-Dawley and 45 male spontaneously hypertensive rats (SHR) body weight (180-200 g) were used in this study. All animals fed commercial laboratory chow and water ad libitum.

Two-kidney one clip Goldblatt hypertensive rats (2K1CGHR); Rats were anesthetized with nembutal (i.p. 30 mg/kg). A 3 cm incision was made on the left flank parallel to the left para median line, and then the abdominal viscera were separated by light traction. Visible nerve fibers separated carefully. After separation a silver clip was applied to the left renal artery.

### *Blood pressure measurement*

Systolic arterial blood pressure measured by tail-cuff method using animal study unit (Narco-Bio system, Huston, Texas, U. S. A.).

### *Hormone assay*

Rats were decapitated and blood was collected into chilled tubes containing EDTA (5 mg/ml, soybean trypsin inhibitor (SBTI, so BAE/ml), and aprotinin (200 KIU/ml). Plasma for hormone analyses was separated from the blood by centrifugation (4°C, 15 min, 3000 rpm). Plasma renin activity (PRA) was determined by radioimmunoassay (RIA) of angiotensin I (AI) (Lee et al, 1991, 1993) and expressed as nanogram Angiotensin I per milliliter per hour (ngAI/ml/hr). Plasma atrial natriuretic peptide (ANP) measured by RIA as described previously (Cho et al, 1989). Plasma aldosterone concentration (PAC) measured by commercial RIA kit (DPC, BA, CA, U. S. A.).

### *Statistical analysis*

Statistical significance was tested using Student's t-test and the results were given as mean±SE.

## Results

Systolic blood pressure (SBP) was significantly decreased during 2 weeks in two-kidney one clip Goldblatt hypertensive rats (2K1CGHR) by Shou-Di-Huang (SDH) compared to control period (Table 1). In the control 2K1CGHR without treatment, there was significant increase up to 3 weeks. Steamed *Rehmanniae* water extract (RWE) decreased blood pressure in 2K1CGHR but there was not significant changes compared to control period.

There was not consistent trend in treatment of SDH and *radix aconiti* (RA) on

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Table 1. Changes in systolic blood pressure after gastric administration of Shou-Di-Huang and Radix Aconiti water extract in two-kidney one clip Goldolatt hypertensive rats (2K1CGHR)

2K1CGHR Group (treated regents)	Systolic blood pressure (mmHg)			
	0	1	2	3 week
Control	168.3±3.5	175.1±3.7*	178.6±3.2*	188.3±3.8*
Shou-Di-Huang	177.4±6.5	168.2±5.6**	162.4±5.0***	166.6±6.6*
Radix Aconiti	177.3±2.9	166.7±2.9	167.3±2.7	165.0±3.7

Values are mean ± SE . 0 weeks; control period (mean of 4 days).\*; significantly different from the control period, \* p < 0.05; \*\* p<0.01; \*\*\* p<0.005

Table 2. Changes in systolic blood pressure after gastric administration of Shou-Di-Huang and Radix Aconiti water extract in spontaneously hypertensive rats

SHR Group (treated regents)	Systolic blood pressure (mmHg)			
	0	1	2	3 week
Control	174.9±2.4	176.2±2.6	180.9±2.1	183.2±2.7*
Shou-Di-Huang	166.9±3.1	170.0±3.6	165.0±3.9	178.9±3.6*
Radix Aconiti	162.5±1.9	159.6±4.6	166.4±3.2	163.6±2.6

\*; significantly different from the control period, \*, p < 0.05

Table 3. Changes in plasma renin activity (PRA), plasma levels of aldosterone (PAC) and arterial natriuretic peptide (ANP) after gastric admimstration of Shou-Di-Huang amd Radix Aconiti water extract in 2K1CGH rats and SH rats

Group (treated regents)	Hormone		
	PRA (ngAI/ml/hr)	PAC (pg/ml)	ANP (pg/ml)
2K1CGH rats			
Control	28.9±1.96	237.0±27.3	204.0±12.0
Shou-Di-Huang	43.5±3.62	258.3±48.7	190.2±20.8
Radix Aconiti	31.4±1.98	182.2±33.0	158.7±20.8
SHR			
Control	40.3±2.07	168.4±11.2	173.6±9.8
Shou-Di-Huang	33.7±2.07	309.3±61.0	167.8±17.6
Radix Aconiti	34.4±0.90	182.0±47.0	125.0±6.5

; significantly different from the control group, p < 0.05.

spontaneously hypertensive rats (SHR) (Table 2). But in control SHR without treatment, SBP increased by time.

Table 3 showed the changes of plasma renin activity (PRA), plasma aldosterone activity (PAC) and atrial natriuretic peptide

(ANP) by treatment of SDH and RA in the SHR and 2K1CGHR. In SHR, SDH and RA treatment has significant decrease on the level of plasma renin activity (PRA) compare to control group, while treatment has no effects in 2K1CGHR. SDH treatment increase PAC in both SHR and 2K1CGHR but there was significance only in SHR. A significant decrease was observed on ANP in 2K1CGHR when SDH was treated.

### Discussion

In the non-treated hypertensive rats, systolic blood pressure increased gradually during the same experimental periods. The etiology of renal hypertension was related with Yin deficiency in oriental medicine (Lee, 1985). *Shou-Di-Huang* is the major component of the *Yukmijihwangtang*. It is used to treat renal hypertension. The depressor response of *Yukmijihwangtang* was related with renin-angiotensin-aldosterone system (Lee, 1985).

Renin secretion rate decreased after the unilateral renal arterial infusion of steamed *Rehmanniae* water extract (Lee et al, 1993). *Shou-Di-Huang* water extract have an anti-hypertensive effect was related with the changes of renin-angiotensin-aldosterone system.

In this study, plasma renin activity not changed, but systolic blood pressure decreased after treated of *Shou-Di-Huang* water extract in 2K1CGHRats. *Radix Aconiti* is the major component of the *Palmiukmijihwangtang*. *Radix Aconiti* water extract prevented to the increase of blood pressure in both of hypertensive rats. Plasma levels of atrial natriuretic peptide decreased after treated of *Radi Aconiti*

water extract in two-kidney one clip Golablatt hypertensive rats and spontaneously hypertensive rats.

These results suggest that the depressor response of *Radix Aconiti* water extracts related with the changes of plasma levels of atrial natriuretic peptide and aldosterone.

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