2003. Vol. 24. No. 4. 87-91
Korean Journal of Oriental Medicine

Original Articles

The Effect of *Rheum palmatum* L. and *Rheum undulatum* L. on Rat Thoracic Aorta and Abdominal Aorta

Tack Kim, Hyung-Hwan Kim, Duk-Kyun Ahn[1], Ho-Young Choi

Oriental Medical College, KyungHee University, Jaseng Research Institute of Biotechnology and Bioscience[1]

Objectives : To examine the relaxational response to the water extract of *Rheum palmatum* L. and *Rheum undulatum* L. on rat thoracic aorta and abdominal aorta.

Methods : Segments of thoracic aorta and abdominal aorta obtained from rats immediately after delivery were mounted in organ baths superfused on a polygraph.

Results : We found that the thoracic aorta segments responded to the water extract of genus Rheum with a dose-dependent vasorelaxation. At 10^{-4} M 5-HT, the maximal contraction force was 93.5% of the maximum KCl-response. The 5-HT induced contractions at 10^{-4} M were inhibited by 86.4% and 62.1% after addition of the high concentrations of *R. palmatum* root (RPR) and leaf (RPL) and *R. undulatum* root (RUR) and leaf (RUL). At 10 mg/ml RPR and RUR, the relaxational response at thoracic aorta and abdominal aorta with and without endothelium were 86.4%, 83.2%, 85.8%, and 62.1% of the maximum 5-HT induced contraction.

Conclusion : Our result showed that RPL and RUL induced dose-dependent vasorelaxation on rat thoracic aorta and abdominal aorta, and that RPL and RUL roots have more potent effects than the leaves. *(Korean J of Oriental Med 2003;24(4):87-91)*

Key Words: *Rheum palmatum* L., *Rheum undulatum* L., 5-Hydroxytryptamine

Introduction

The dried root of *R. palmatum* and *R. undulatum* have long been used in traditional Chinese medicine. It has been reported for treatment of hypertension, lipemia, and paramenia in the oriental herbal medicines for a long time[1-4].

There have been reports that *R. palmatum* root given to anesthetized dogs lowered their blood pressure. The effects of emodin, one of main components in *R. palmatum* and *R. undulatum*, on the isolated intestinal smooth muscle of guinea pigs were dose dependent[5].

In this study, we focused on vasorelaxational effect of *R. palmatum* and *R. undulatum* cultivated in Korea. In order to study the vasodilation effect, we have in the present study characterized the relative relaxational response to water extract of *R. palmatum* and *R. undulatum* (root and leaf) on rat thoracic aorta and abdominal aorta.

Received 16 October 2003; revised 25 October 2003; accepted 2 November 2003

Correspondence to:Ho-Young Choi, Oriental Medical College, KyungHee University, Seoul 130-701, Korea; Tel: 82-2-961-9372, Fax: 82-2-965-9372, E-mail: hychoi@khu.ac.kr

Materials and Methods

1. Plant Material

1) Plant Origin

The dried roots (RPR) and leaves (RPL) of *R. palmatum* were collected at Pyunchangsanchesihumjang

(in Kangwon-do, Korea), and the dried roots (RUR) and leaves (RUL) of *R. undulatum* were collected at Pukbunongupsihumjang (in Kangwon-do, Korea).

2) Preparation and Handling of *R. palmatum* and *R. undulatum*

Water extracts of *R. palmatum* and *R. undulatum* were prepared from dried roots and leaves cultivated in Korea. They were cut into small pieces and mashed with a mortar and pestle. The roots (100 g) were extracted with boiling water (50 g/L), total volume 2L. The extract of *R. palmatum* and *R. undulatum* was dissolved in 1 ml of distilled water.

2. Animals

Adult male Sprague-Dawley rats (SD, 300-350 g) were used for the present study. Animals were purchased from Semtaco Animal Care (Semtaco, Korea) and housed and cared for in accordance with the Guide for the Care and Use of Laboratory Animals.

3. Materials

NaCl, KCl, NaH_2PO_4, $MgSO_4$, $CaCl_2$, $NaHCO_3$, glucose, 5-HT and Acetylcholine were purchased from Sigma (Sigma, USA).

4. Preparation of isolated aortic rings

Male SD rats were killed with an overdose of chloral hydrate (400 mg/kg, ip) and the thoracic aorta and mesenteric artery were removed and cleaned of adherent tissue. The aorta and mesenteric artery were mounted on a length of scoured polythene tubing and placed in a petri dish containing modified physiological salt solution (PSS) of the following composition (mM): NaCl 119.0, $NaHCO_3$ 25.0, KCl 4.7, KH_2PO_4 1.2, $MgSO_4$ 1.2, glucose 11.0, $CaCl_2$ 0.25. The aorta was cleared of surrounding adipose tissue and the endothelium was removed by gentle rubbing of the intimal surface with the polythene tube. Six to nine ring segments (2-3 mm length) were prepared from each aorta and were mounted between two stainless-steel wires in 5 ml organ baths, thermostatistically controlled at 37 ℃, containing modified PSS. The solution was bubbled with a gas mixture consisting of 95% O_2 and 5% CO_2 in order to keep a pH in the bath of around 7.35-7.38. Experiments were carried out after the vessel had equilibrated, usually within 1-2 h of mounting.

The tension was recorded isometrically with a Grass FT03C force-displacement transducer and registered on a Grass model 7 polygraph. The vessels were given an initial passive load of about 2 g and allowed to equilibrate for at least 90 min prior to the experiments. After the equilibrating period, vessels were stimulated with KCl (100 mM) in order to obtain a reference contraction. This contraction was defined as the maximal contraction to KCl. Vessels that did not respond or responded abnormally were not tested further. RPR, RUR, RPL, and RUL and other substances were dissolved in 0.9% NaCl and given to the baths in volumes of 5 mL. The response to the added substances (contraction or relaxation) was expressed as a percentage of the maximal KCl-induced contraction exhibited by each ring. After the resting tension became stabilized, 5-HT were administrated into the bathing buffer to induce a rapid increase of vascular tone followed by the stable vasoconstriction. Treatments groups were administered RPR, RUR, RPL, and RUL from concentrations of 10^{-4} to 100 mg/ml to observe vasodilation (the decrease of tonic contraction). Concentration-relaxation curves were generated in a cumulative fashion.

5. Statistical analysis

Analysis of data from the two groups was performed using Student' s *t*-test.

Data from several groups were examined using analysis of variance (ANOVA), using the computer

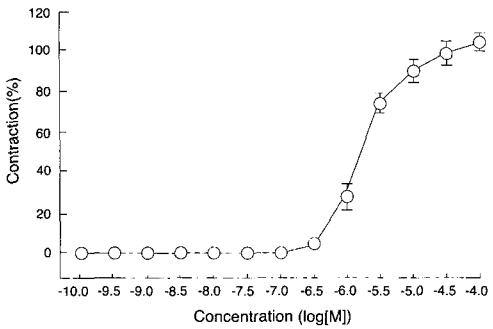

Fig. 1. Contractile response of 5-HT (○) at concentration ranging from 10^{-10} M to 10^{-4} M. Results represent mean±SEM on the maximal contractional response.
On the X-axis: log[M] ; on the Y-axis: contraction (%). n=5-6.

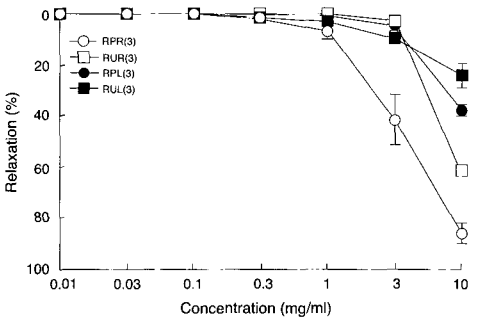

Fig. 2. RPR, RUR, RPL, and RUL caused concentration-dependent relaxation in the 10^{-4} M 5-HT induced contraction of rat thoracic aorta without endothelium.
RPR, *R. palmatum* root; RUR, *R. undulatum* root; RPL, *R. palmatum* leaf; RUL, *R. undulatum* leaf.
Data represent mean ± SEM. n=3.

Table 1. Rmax and EC_{50} Values of the Relaxation to Extract of RPR, RPL, RUR, and RUL in Rat Thoracic Aorta

	Thoracic Aorta	
	Rmax (%)	EC_{50} (mg/ml)
RPL	86.4 ± 3.9	5.22
RUL	62.1 ± 1.3	8.77
RPL	37.6 ± 2.3	-
RUL	24.5 ± 4.6	-

RPR, *R. palmatum* root; RUR, *R. undulatum* root; RPL, *R. palmatum* leaf; RUL, *R. undulatum* leaf; EC_{50}, the concentration required to produce 50% of the maximal response; Rmax, maximal response.
Data are mean ± SEM. n=3.

program GraphPad Prism (GraphPad Software, San Diego, CA). Significance levels were set as follows: p=0.05(*), p=0.01(**), p=0.001(***).

Results

1. Effect of 5-HT induced contraction

5-HT (10^{-8}-10^{-4} M) produced a concentration-dependent and dose-dependent contraction of the thoracic aorta. At 10-4 M 5-HT, the maximal contractile response were 93.5±3.3% of the maximum KCl-response, and EC_{50} was 0.81×10^{-5} M(Fig. 1).

2. Inhibition Effect of RPR, RUR, RPL, and RUL on 5-HT induced contraction

Thoracic aorta segments responded to 5-HT with a dose-dependent vasoconstriction. At 10 mg/ml RPR, RPL, RUR, and RUL, the relaxational response were 86.4±3.9%, 37.6±2.3%, 62.1±1.3% and 24.5±4.6% of the maximum 5-HT induced contraction and EC_{50} of ERP-R and ERU-R were 5.22 mg/ml and 8.77 mg/ml (Fig. 2, Table 1).

3. Effect of RPR and RUR on 5-HT induced contraction in rat thoracic aorta with and without endothelium

Inhibitional effect of RPR and RUR on 5-HT induced contraction was dose-independent. At 10^{-4} M 5-HT, the relaxational response of RPR and RUR with and without endothelium were 86.4%, 83.2%, 85.8%, and 62.1% of the maximum KCl-response (Fig. 3).

Discussion

Rhizoma Rhei originated from *R. palmatum* L., R. tanguticum Maxim. et Reg., R. officinale Baill. *R. undulatum* L. is also used as Rhizoma Rhei in Korea. Rhizoma Rhei was described at the first phytology text, Divine Husbandman' s Classic of the Materia Medica. Its properties are bitter and cold. Its channel enters the

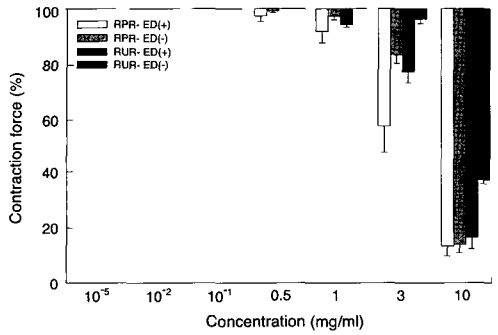

Fig. 3. RPR and RUR caused concentration-dependent inhibition response in the 10^{-4} M 5-HT induced contraction of rat thoracic aorta with and without endothelium.
RPR, *R. palmatum* root; RUR, *R. undulatum* root.
Data represent mean ± SEM.

stomach, large intestine and liver. Its function is mainly to drain heat and move stool. One of the important functions is to clear heat obstructing the blood level. The other function is to invigorate the blood and break up congealed blood. It has drain-heat and move-stool functions and is used for high fever, profuse sweating, thirst, constipation, abdominal distension and pain, delirium, yellow tongue moss, and a full pulse[1-4].

In pharmacological and clinical research, cardiovascular effects include infusions and tinctures of Rhizoma Rhei given to anesthetized dogs which lowered their blood pressure[5].

Extract of Rhizoma Rhei can suppress the production of tumor necrosis factor and interleukin-1 by macrophages as well as interleukin-6 by human mesangial cells. It is reported that emodin possesses antibiotic and antineoplastic functions. It has an effect on the pathogenicity of trichomonas vaginalis in mice[6-14]. The effect of emodin action on the isolated intestinal smooth muscle of guinea pigs was dose dependent[5].

Small doses stimulated frog' s hearts, while larger doses inhibited them.

The present results indicate that the water extract of the roots of *R. palmatum* and R. tanguticum does possess relaxation effects in rat thoracic aorta and abdominal aorta.

A number of agents have been shown to relax vascular smooth muscle through release from the endothelium of a labile relaxing factor. This indirect relaxation is generally detected by comparing responses of intact and endothelium-denuded isolated vascular preparations. Water extract of the roots of *R. palmatum* and R. tanguticum inhibited 5-HT induced contractions in thoracic and abdominal aortic rings with and without endothelium, suggesting an effect exerted directly on smooth muscle.

In conclusion, our result showed that *R. palmatum* and R. tanguticum induced dose-dependent vasorelaxation on rat thoracic aorta and abdominal aorta and that the roots of *R. palmatum* and R. tanguticum have more potent effect than the leaves.

References

1. Ahn DK. Illustrated Book of Korean Medicinal Herbs. Kyo-Hak Publishing Co. 1998:274-275.
2. Lee YN. Flora of Korea. Kyo-Hak Publishing Co. 1998:98-99.
3. Huang KC. The pharmacology of Chinese herbs. CRC Press. 1999:234.
4. Bensky D et al. Chinese Herbal medicine. Eastland Press. 1992:166-168.
5. Jin ZH, Ma DL, Lin XZ. Study on effect of emodin on the isolated intestinal smooth muscle of guinea-pigs. *Zhongguo Zhong Xi Yi Jie He Za Zhi.* 1994;14(7):429.
6. Wang HH.. Antitrichomonal action of emodin in mice. *J. Ethnopharmacol.* 1993;40(2):111-116.
7. Wang S, Fan M, Bian Z. Experimental study of bacteriostatic activity of Chinese herbal medicines on primary cariogenic bacteria in vitro. *Zhonghua Kou Qiang Yi Xue Za Zhi.* 2001;36(5):385.
8. Kim TG, Kang SY, Jung KK, Kang JH, Lee E, Han HM, Kim SH. Antiviral activities of extracts isolated from Terminalis chebula Retz., *Sanguisorba officinalis*

L., Rubus coreanus Miq. and *Rheum palmatum* L. against hepatitis B virus. *Phytother Res.* 2001; 15(8):718.

9. Zhang Q, Zhang C, Wang J, Guan L, Yu H. Effect of Rheum palmatum decoction on increasing intelligence. *Zhong Yao Cai.* 2001;24(10):728.
10. Cuellar MJ, Giner RM, Recio MC, Manez S, Rios JL. Topical anti-inflammatory activity of some Asian medicinal plants used in dermatological disorders. *Fitoterapia.* 2001;72(3):221.
11. Song H, Wang Z, Zhang F. Investigation of urinary interleukin-6 level in chronic renal failure patients and the influence of *Rheum palmatum* in treating it. *Zhongguo Zhong Xi Yi Jie He Za Zhi.* 2000;20(2):107.
12. Bae EA, Han MJ, Kim NJ, Kim DH.. Anti-Helicobacter pylori activity of herbal medicines. *Biol Pharm Bull.* 1998;21(9):990.
13. Kim DH, Park EK, Bae EA, Han MJ. Metabolism of rhaponticin and chrysophanol 8-o-beta-D-glucopyranoside from the rhizome of *Rheum undulatum* by human intestinal bacteria and their anti-allergic actions. *Biol Pharm Bull.* 2000;23(7):830.
14. Hisashi M, Tadashi K, Toshio M, Iwao T, Shoichi H, Masayuki Y. Effects of Stilbene Constituents from Rhubarb on Nitric Oxide Production in Lipopolysaccharide-Activated Macrophages. *Bioorganic & Medicinal Chemistry Letters.* 2000;10:323.