EFFECT OF KOREAN RED GINSENG POWDER (GP), ADMINISTERED ORALLY, ON BLOOD PRESSURE IN HYPERTENSIVE RATS

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INTRODUCTION

Korean ginseng has been regarded as both prohypertensive and antihypertensive for many years[1]. Acute and chronic experiments in animals with ginseng are also controversial, suggesting again both prohypertensive and antihypertensive[1].

Dr. E.S. Sohn and his collaborators in this country reported at the last Symposium that in the spontaneously hypertensive rats (SHR) ginseng appeared prohypertensive at smaller dosis, whereas it is antihypertensive at larger dosis[1,2]. The route of administration they used was intraperitoneal and oral. They also studied plasma renin activity, which is decreased after ginseng treatment in parallel with BP decrease[1,2].

In the present study, we have investigated the effect of Korean red ginseng powder, given orally, on blood pressure (BP) in hypertenisve rats. Ginseng powder (Korai Kosanfun in Japanese) was obtained from the Japan Korea Red Ginseng Co. Preliminary and detailed reports have been presented elsewhere[3-6].

MATERIALS AND METHODS

Table 1 shows the experimental groups investigated. Both chronic and acute experiments were carried out in two series, Study 1 and 2. Normotensive Donryu strain, spontaneously hypertensive, two kidney, one clip hypertensive (CLIP), severly or mildly hypertensive with deoxycorticosterone and salt (DOC(s)) and (DOC (m)), and stroke-prone SHR (SHRSP) rats were used for chronic experiments. They were either treated with ginseng or untreated, indicated as control, for 11 weeks. Ginseng powder was mixed into the pellets, which were taken *ad libitum* by rat. Doses of ginseng ranged 250-700mg/kg per day.

Table 1. Experimental groups

Rat	Treatment	No. of Rats
(Chronic)		
Study 1		
DON	Control	11
DON	GP	11
SHR	Control	10
SHR	GP	11
CLIP	Control	10
CLIP	GP	10
DOC(s)	Control	11
DOC(s)	GP	10
Study 2		
DOC(m)	Control	7
DOC (m)	GP	9
SHRSP	Control	10
SHRSP	GP	8
(Acute)		
SHRSP	Control	5 x 2
SHRSP	GP	5 x 2
DOC	Control	5 x 2
DOC	GP	5 x 2

DOC and SHRSP rats were used for acute experiments in study 2. GP is given orally by a gastric tube at a dose of 350mg/kg. All rats used in Study 1 and 2 were female except SHRSP rats. Both direct and indirect methods were used for BP determination[6]. In the direct determination, the abdominal aorta is cannulated through the femoral artery. The cannula is connected to a strain gauge transducer, and mean BP was recorded directly without anesthesia or restraint. As the cannula is sometimes clotted, this method can not be used for a longer duration. It was used in acute experiments, and at the end of the chronic experiments. The indirect determination was carried out by so-called "tail cuff" method. BP is obtained at the tail without anesthesia, but prewarming is necessary. We performed it at 50°C for 3min. However, a recent study indicated that prewarming on a hot plate at 35°C for 30-60 min is less stressfull. Apparatuses used in Study 1 and 2 were KN-209 and KN-210, respectively. The difference is in that BP is determined while cuff pressure is decreasing or increasing. Consequently, BP values obtained by KN-209 and KN-210 were near mean and maximum, respectively.

In the chronic studies, a blood sample of 0.5ml was obtained following BP determination. Plasma renin activity was determined by the modified method of Carvalho et al[6].

RESULTS

Study 1

In the first series of experiments, several representative types of hypertensive rats: SHR, CLIP, DOC in parallel with normotensive DON rats were used. Fig. 1 shows BP curves of DON rats. The experiment was started at age of 8 wk. Ginseng administration resulted in no effect on BP. Food and fluid intakes, body weight, heart rate, heart and kidney weights were not affected with ginseng.

Fig. 2 is the BP curves of SHR, from the colony of our Department, at age of 8 wk. BP was increasing, at this age, but ginseng treatment

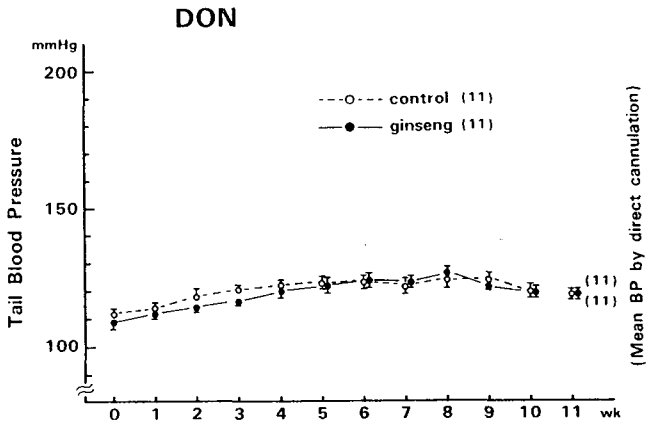

Fig. 1. Chronic effects of ginseng (340-685mg/kg, p.o.) on BP in normotensive Donryu (DON) rats. Near mean (tail) BP was determined by a rat tail manometer-tachometer system (Natsume KN-209). Vertical bars are S.E. of the mean. Initial and final No. of rats in each group are shown in parentheses following explanation for symbols and at the last week of the observation, respectively.

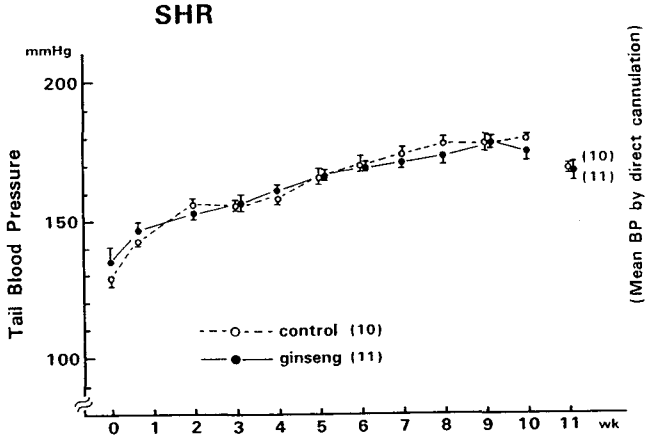

Fig. 2. Chronic effects of ginseng (380-595mg/kg p.o.) on BP in spontaneously hypertensive (SHR) rats. Details are the same as in Fig. 1.

did not affect BP curve. Other parameters were not affected either.

Fig. 3 is the BP curves of CLIP rats, two kidney, one clip type. Ginseng administration did not affect either BP curve or other parameters. Incidence of vascular lesions, polyarteritis nodosa and nephrosclarosis, was not changed.

Fig. 4 is the BP curves of DOC rats, deoxycorticosterone and salt hypertension. Hypertension was rather accerelated in this series, with deoxycorticosterone 8mg/kg per week subcu-

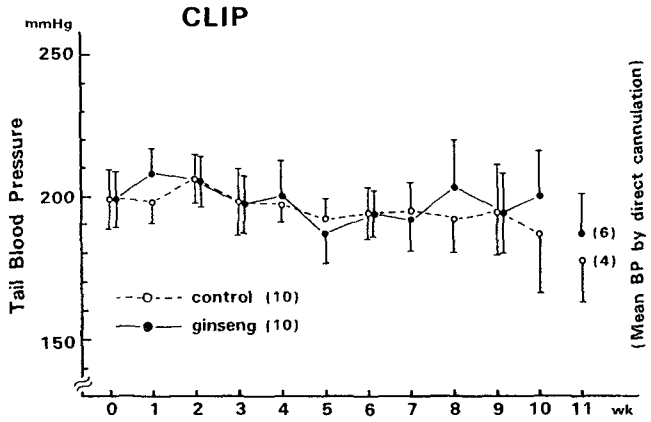

Fig. 3. Chronic effects of ginseng (365-425mg/kg p.o.) on BP in two kidney, one clip (Clip) rats. Details are the same as in Fig. 1.

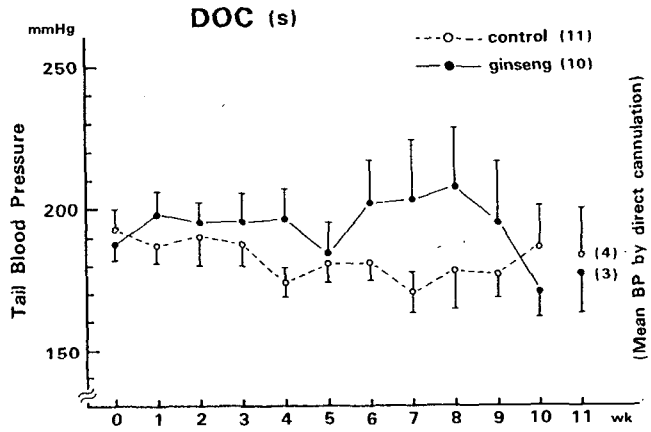

Fig. 4. Chronic effect of ginseng (275-350mg/kg, p.o.) on BP in severely hypertensive deoxycorticosteron (DOC(s)) rats. Details are the same as in Fig. 1.

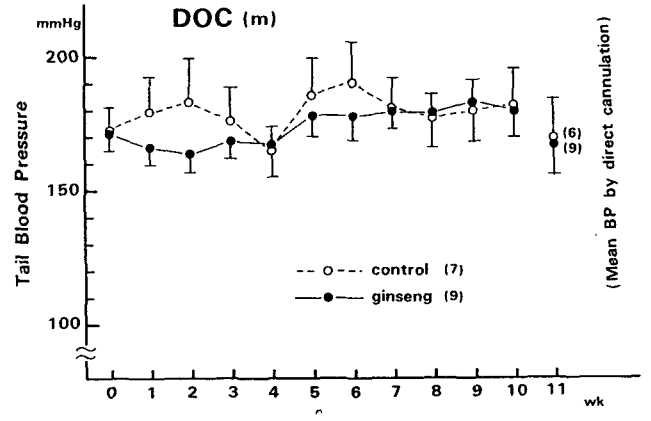

Fig. 5. Chronic effects of ginseng (330-395mg/kg, p.o.) on BP in mildly hypertensive DOC (DOC(s)) rats. Maximum (tail) BP was determined by a new rat tail manometer - tachometer system (Natsume KN-210). Other details are the same as in Fig. 1.

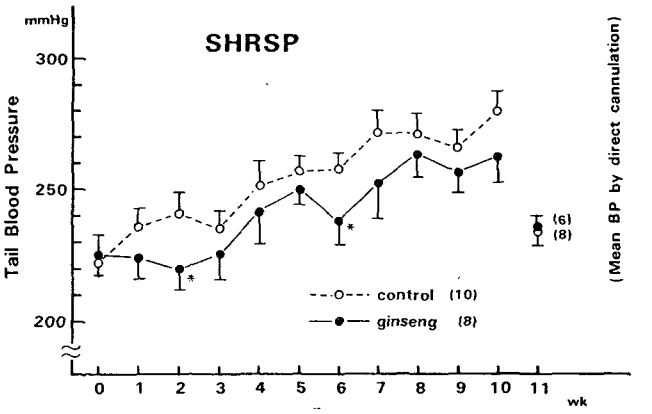

Fig. 6. Chronic effects of ginseng (395-465mg/kg, p.o.) on BP in stroke-prone SHR (SHRSP) rats. Details are the same as in Fig. 5. *indicates statistically significant difference ($P<0.05$), compared to the control.

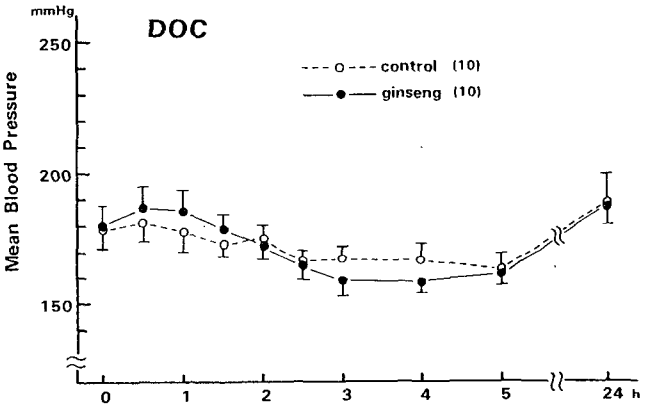

Fig. 7. Acute effects of ginseng (350mg/kg, p.o.) on mean BP in DOC rats. BP was determined through a cannula inserted into the abdominal aorta without anesthesia or restraint.

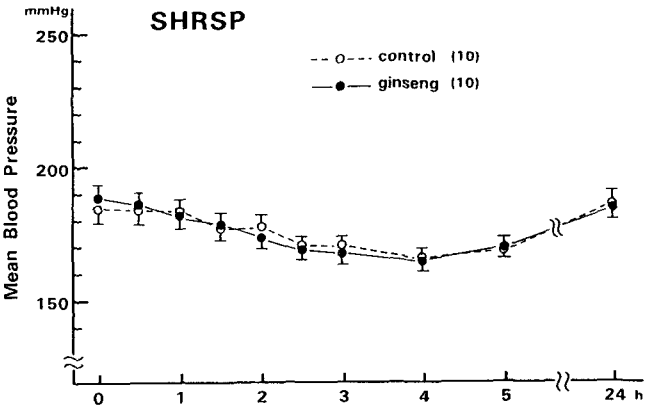

Fig. 8. Acute effects of ginseng (350mg/kg, p.o.) on mean BP in SHRSP rats. Details are the same as in Fig. 7.

Table 2. Effects of ginseng on plasma renin concentration (PRC)

Rat	Treatment	No. of Rats	PRC (angiotensin I formation) ng/ml per h	P
DON	Control	11	17.7 ± 2.8*	–
	ginseng	11	19.0 ± 1.7	NS**
SHR	control	10	11.6 ± 0.7	–
	ginseng	11	14.9 ± 1.9	NS
CLIP	control	4	89.6 ± 42.3	–
	ginseng	6	291.3 ± 157.1	NS
DOC(s)	control	4	8.2 ± 0.9	–
	ginseng	3	7.9 ± 1.2	NS
DOC(m)	control	6	3.2 ± 1.5	–
	ginseng	9	2.9 ± 1.1	NS
SHRSP	control	8	50.1 ± 3.0	–
	ginseng	6	35.6 ± 9.3	NS

* Mean ± SE ** Statistically not significant compared to control

taneously, and we called as severly hypertensive DOC (DOC(s) rats. Early death in some rats with higher BP in control group resulted in slightly higher BP. But the differences were not statistically significant. Lower BP in the treated group at the 10th week was due to death of rats with higher BP. Therefore, we repeated the experiment in DOC rats in the second series. Ginseng treatment increased 1% saline intake and heart rate, and decreased food intake and body weight. However, relationship of BP and these parameters was unknown.

Study 2

Fig. 5 is the BP curves of DOC rats in the second series. Dosis of deoxycorticosterone was reduced to 5-7mg/kg before and 3mg/kg after the ginseng treatment. Hypertension was relatively mild in this series, and called as mildly hypertensive, DOC(m). No appreciable effect was seen. The treated group showed relatively lower BP in this series in the early phase. Ginseng treatment might be favorable to the prewarming stress in BP determination. Heart rate was increased through out the experiment. Fluid intake was also increased later phase of the experiments. From the result on DOC rats of the first and second series we concluded that ginseng has no appreciable effect on BP.

Fig. 6 is the BP curves of SHRSP rats. The experiment started at the age of 12 weeks. The treated group showed lower BP. The differences became significant at the 2nd and 6th week. However, mean BP values determined directly were not different, indicating that prewarming stress increased BP, and that ginseng treatment had favorable effect on it. Vascular lesions were not prevented by the ginseng treatment.

Table 2 shows effects of ginseng on plasma renin activity in the chronic experiments. Ginseng treatment did not change this activity in either group of normotensive and hypertensive rats.

In study 2, we determined acute effect of ginseng on BP for 24 hr. Ginseng was given by a gastric tube in a dose of 350mg/kg. As seen from BP cureves in Fig. 7, ginseng had no appreciable effect acutely in DOC rats. Fig. 8 is the acute effects on BP of ginseng in SHRSP rats. Ginseng had no effect.

DISCUSSION

Our detailed studies using one normoten-

sive and four different types of hypertensive rats resulted in essentially negative effects on BP, acutely and chronically. Discrepancies between previous positive reports, especially those of Sohn and others in SHR rats, and the present studies may be due to differences in methods of BP determination, and of administration of ginseng, strain of SHR rat, etc. Further studies are necessary to confirm these differences.

In summary then, Korean red ginseng powder showed no appreciable antihypertensive effect in SHR, CLIP, DOC, or SHRSP rats in the chronic experiments. Ginseng was given orally at doses of 250-700mg/kg per day for 11 weeks. In the acute experiments, ginseng powder showed no appreciable effect on blood pressure in DOC or SHRSP rats for 24 hr, when given orally at a dose of 350mg/kg.

ACKNOWLEDGEMENTS

We thank Ms. Yukie Kurihara, Ms. Yuko Nakajima, and Ms. Kuniko Haga for technical and secretarial assistances.

Chong: One of your first slides on hypertension showed that ginseng actually cause the blood pressure to rise in DOC rats but you thought it was not statistically significant.

Sokabe: Your point is right. In the first series of DOC rats with relatively, severe hypertension, it seems that ginseng treatment caused blood pressure to rise. But if you look at the data carefully, the blood pressure of control rats is also high because of the early death of some rats in control group. Therefore, our conclusion is that ginseng treatment doesn't cause blood pressure to rise.

Chong: Instead of measuring blood pressure in the tail by using cuff method which is slightly inaccurate, perhaps it might be better to use pressure transducers.

Sokabe: Thank you for your nice suggestion but as I have shown on the slide, at the end of the experiment we cannulated the aorta and measured blood pressure directly. However, the tube sometimes got closed so we couldn't use this method throughout the experiment.

홍삼분말이 고혈압 쥐에 미치는 영향

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이미 발표된, 혈압에 미치는 인삼의 효과에 관한 연구들의 보고는 서로 상반된 견해들이 많이 있다. 인삼에는 혈압상승작용과 혈압을 내려주는 효과가 모두 있다고 보고하였다.

본 저자들은 고혈압 쥐에 미치는 인삼의 급·만성 효과를 연구하기 위해 일련의 2가지 실험을 하였으며, 실험재료로 사용한 홍삼은 일한홍삼주식회사에서 구입하였다.

(실험 1)

홍삼분말을 일반 쥐사료에 혼합하여(5g/kg), 임의로 사료를 섭취하게 하여 11주간 쥐를 사육하였으며, 하루에 섭취한 인삼의 양은 체중 kg당 250~700mg이었다. 홍삼분말의 투여는 DON쥐, SHR쥐, 그리고 한개의 신장을 협자시킨 고혈압 쥐의 경우 혈압에 영향을 미치지 않았다. 홍삼분말의 투여는 DOC 쥐에 있어 혈압을 약간 상승시켰다.

(실험 2)

홍삼분말을 체중 kg당 350mg씩 경구투여한 후 복대동맥에 카뉼제를 삽입하여 혈압을 24시간 직접 측정하였다.

그 결과 DOC쥐와 SHRSP쥐에 있어 혈압에 영향이 없었다.

이 실험에서는 마취를 시키지 않았으며, 자유로이 풀어 놓았다.

실험 1과 같이 매일 체중 kg당 300~500mg씩 11주간 홍삼분말을 만성적으로 투여하였을 때, SHRSP쥐의 혈압에 영향이 없었다.

DOC 고혈압 쥐의 경우 약간의 혈압 강하가 있었으며, DOC 고혈압의 정도는 (실험 2)에서 약간 낮았다.

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