

Original Article

Clinical Effects of Korean Ginseng, Korean Red Ginseng, Chinese Ginseng, and American Ginseng on Blood Pressure in Mild Hypertensive Subjects

Dong-Jun Choi, Ki-Ho Cho¹⁾, Woo-Sang Jung¹⁾, Seong-Uk Park²⁾
Chang-Ho Han, Won-Chul Lee

Department of Oriental Internal Medicine, International Hospital
Dong-Guk University Goyang-city, Gyeonggi-do, Korea
Department of Cardiovascular and Neurologic Diseases (Stroke Center)
College of Oriental Medicine, Kyung-Hee University, Seoul, Korea¹⁾
Stroke & Neurological Disorders Center, East-West Neo Medical Center
Kyung-Hee University, Seoul, Korea²⁾

Background : Ginseng has traditionally been used in oriental countries to recover vital energy from Qi deficiency, and has shown various biomedical effects in the scientific literature. Recent reports suggest that ginseng could regulate blood pressure (BP), but much controversy still remains. Therefore, we intended to assess the anti-hypertensive effect of several ginseng types frequently used in clinics. We also investigated the anti-hypertensive effect on Koreans and Chinese, and by the body type according to *Sasang* Constitution Medicine (SCM).

Methods : The study subjects were recruited from mildly hypertensive patients who exhibited pre-hypertension (120/80 to 139/89 mmHg) and stage I hypertension (140/90 to 159/99 mmHg) in Korea and China. After assigning the subjects into a Korean, a Chinese, a red, and an American ginseng group by randomization, we prescribed ginseng at a dose of 4.5 g per day for 4 weeks. To assess the anti-hypertensive effect, we compared the mean of systolic and diastolic BP between before and after ginseng medication using a 24-hour ambulatory blood pressure monitor (24 hr ABPM). We also monitored adverse effect and laboratory findings to secure the subjects' safety. In addition, all of the subjects in Korea consulted a specialist of *Sasang* Constitution Medicine to identify their constitutional type.

Results : There were 64 subjects treated with Korean ginseng, 58 treated with Chinese ginseng, 33 treated with red ginseng, and 64 treated with American ginseng. Korean, Chinese, and American ginseng all reduced subjects' BP. Korean and Chinese ginseng showed more effect. The secondary analysis on the subjects' nationality revealed that all of the ginseng types showed more significant anti-hypertensive effect in Chinese patients than in Koreans. The third analysis on the constitutional type of SCM showed there was no significant difference in the effectiveness and the safety of ginseng among the constitutional types.

Conclusions : We suggest ginseng, especially *Panax ginseng* without any steaming-drying process, could be useful for mild hypertension. Further, ginseng is safe regardless of subjects' constitutional type or type of ginseng within a dosage of 4.5 g per day.

Key Words : blood pressure, ginseng, hypertension

Introduction

For thousands of years, herbs have been used in various medical fields in Asia. In spite of their actual effectiveness, many of them have not yet been fully understood or appreciated by western biomedicine. However, their mechanism and applications have appeared with increasing

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corresponding author : Ki-Ho Cho

Assistant Professor, Department of Cardiovascular & Neurologic Disease (Stroke Center), Hospital of Oriental Medicine, Kyung Hee Medical Center. 1 Hoegi-dong, Dongdaemun-gu, Seoul # 130-702, Korea
Tel : 82-2-958-9125 / FAX : 82-2-958-9132
E-mail : cdjuni@yahoo.com

frequency in literature of basic and clinical science.

Ginseng is one of them. According to oriental medical theory, it is believed to have aphrodisiac and beneficial effect on energy deficiency of human beings by relieving fatigue, mental and nervous exhaustion. It is helpful for increasing quality of life by improving the body's resistance to stress and increasing vitality^{1,2)}.

Previous studies revealed that ginseng has anti-oxidative effect³⁻⁵⁾, anti-cancer effect⁶⁻⁸⁾, anti-stress effect⁹⁾, and anti-aging effect¹⁰⁾. It also has various biomedical effects on the digestive function^{11,12)}, cognitive function^{13,14)}, muscular function¹⁵⁾, immune system^{16,17)}, endocrine system¹⁸⁻²⁰⁾, reproductive system^{21,22)}, and vascular system²³⁻²⁵⁾.

Recently, the possibility that ginseng could regulate blood pressure has been suggested. In the experimental studies, ginseng decreased blood pressure and pulse rate in hypertensive rats²⁶⁾, and improved pulmonary hypertension by reducing vascular resistance and elevating cardiac output²⁷⁾. In clinical studies, ginseng increased forearm blood flow measured by plethysmography²⁸⁾, and relaxed myocardial function by inhibiting intracellular calcium overload and reducing left ventricular muscle mass²⁹⁾. Furthermore, in a randomized controlled clinical trial with 24-hour ambulatory blood pressure monitor, it showed significant anti-hypertensive effect compared to the control³⁰⁾.

The most popular types of ginseng are Korean ginseng, Chinese ginseng, red ginseng and American ginseng. Korean and Chinese ginseng are raw 4-year-old *Panax ginseng* roots. Korean ginseng is grown in Korea, while Chinese ginseng is grown in China. Red ginseng is a product made by applying some processing to 6-year-old *Panax ginseng* roots. Six-year-old

fresh raw ginseng is carefully selected, washed thoroughly with spring water, steamed, sun-dried and pressed into a pine box. Thereafter, it can be stored as long as 10 years without denaturing its active ingredients or losing its pharmacological activity. American ginseng is raw 4-year-old *Panax Quinquefolium* roots. These are now used indiscriminately because little is known about differences between the species.

Therefore, we intended to assess the clinical anti-hypertensive effect of ginseng on hypertension, and compare the effect among ginseng types. We also investigated the anti-hypertensive effect by nationality on Koreans and Chinese, and by body type according to *Sasang* Constitution Medicine (SCM).

SCM, developed by Lee Je-ma in the 19th century, is one the unique branches of Korean Oriental Medicine (KOM), and claims that human constitutions can be classified into four constitutional types based on a synthetic judgment of each individual's physique, behavior, and response to herbal medication: *Tae-yang*, *So-yang*, *Tae-eum*, and *So-eum*. SCM has been further developed and is now practiced in Korea by almost all traditional doctors^{31,32)}. Because, under SCM, ginseng belongs to the list of *So-eum*'s medicines, specialists of SCM advise ginseng should be prescribed primarily to those of *So-eum* type. However, much controversy still exists around this.

Methods

1. Subjects

The population of this study was based on northeast Asia: Korea and China. We included patients with mild hypertension in which blood pressure (BP) ranged from 120/80 mmHg to 159/99 mmHg. These belong to pre-hypertension and

Table 1. Remaining agricultural chemicals from Korean, Chinese, Red, and American Ginseng used in This Study.

Agricultural chemicals name	Permitted limit (ppm)	ChG	AmG	KG	KRG
BHC	0.2	0.007	ND	ND	ND
DDT	0.1	ND	ND	ND	ND
Aldrin/Dieldrin	0.01	ND	ND	ND	ND
Endrin	0.01	ND	ND	ND	ND
Quintozene	1.0	0.009	0.590	0.107	0.008
Endosulfan	0.2	ND	ND	0.099	0.056
Captan	2.0	ND	ND	ND	ND
Parathion	0.1	ND	ND	ND	ND
Diazinon	0.1	ND	ND	ND	ND
Metalaxyl	1.0	-	-	-	-
Carbendazim	0.5	-	-	-	-
Deltamethrin	0.02	ND	ND	ND	ND
Diethofencarb	0.5	ND	ND	ND	ND
Cypermethrin	0.1	ND	ND	ND	ND
Azoxystrobin	0.5	ND	ND	ND	ND
TolyFluanid	0.3	ND	ND	ND	ND
Tolclofosmethyl	1.0	0.012	ND	0.088	0.055
Difenoconazole	0.2	ND	ND	ND	ND
Procymidone	0.4	ND	ND	0.400	0.214

Limits are based upon standard of dry ginseng

ChG: Chinese ginseng, AmG: American ginseng, KG: Korean ginseng, KRG: Korean red ginseng, BHC: benzene hexachloride, DDT:dichloro-diphenyl-trichloroethane, ND: not detected.

stage I hypertension according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) Express. In Korea, we recruited 123 subjects at the Department of Cardiovascular & Neurologic Diseases (Stroke Center) of Kyung Hee Oriental Medical Hospital, from June 2004 to October 2004, and in China, 96 subjects were recruited at the Emergency Room of the Teaching Hospital of Traditional Chinese Medicine of Chengdu University, from July 2004 to April 2005. Exclusion criteria were severe diabetes mellitus, renal failure, pregnancy, secondary or malignant hypertension, and cardiovascular disease within 3 months.

2. Materials

Ginseng materials were supplied by the Korean

National Agricultural Cooperative Federation (NACF). To guarantee safety, we checked for residue of agricultural chemicals in the materials (Table 1). We then capsulated the materials (375 mg per one capsule) after reducing to powder.

3. Procedures

We included the eligible subjects after assessing general characteristics and their BP by 24-hour ambulatory blood pressure monitor (24 hr ABPM). We then prescribed ginseng at 4.5 g (12 capsules) a day for 4 weeks after assigning the subjects into a Korean, a Chinese, a red, and a American ginseng group by randomization stratified by sex, age, and the mean BP obtained from 24 hours monitoring.

To assess the anti-hypertensive effect of ginseng, we rechecked the subjects' BP by the 24 hr

Table 2. Baseline Assessment according to Ginseng Species.

	Korean ginseng (n=64)	Chinese ginseng (n=58)	Red ginseng (n=33)	American ginseng (n=64)
Age, yr	54.8 ± 9.9	55.0 ± 9.7	50.5 ± 9.7	54.9 ± 10.4
Sex (M/F)	34 / 30	29 / 29	15 / 18	36 / 28
Medical history				
BP medication	19	22	6	23
Diabetes	1	1	3	2
Hyperlipidemia	6	1	3	5
Systolic BP, mmHg	137.3 ± 10.2	136.8 ± 9.3	135.2 ± 9.0	136.5 ± 11.5
Diastolic BP, mmHg	86.7 ± 7.3	85.9 ± 6.5	86.6 ± 6.5	86.6 ± 6.5
VAS on headache	14.5 ± 26.9	9.0 ± 21.3	23.9 ± 30.2	15.2 ± 26.1

There was no significant difference by one-way ANOVA test for continuous variables and chi-square test for categorical variables.

ABPM, and also investigated the effect of ginseng on symptoms related with hypertension (such as headache) after 4 weeks of medication. We also monitored adverse effect and laboratory findings to secure the subjects' safety.

At the end of the protocol, an independent specialist of SCM identified the constitutional type of the subjects with physical examination and the Questionnaire of *Sasang* Constitution Classification (QSCC II), composed of questions about the individual patterns of work performance, strength and weakness, personal relationships, general attitude, personal problems, emotional characteristics, behavioral characteristics, and physical condition^{33,34)}

Informed consent was given by all the subjects after a full explanation of the study, and the Institutional Review Board (IRB) of Kyung Hee Oriental Medical Hospital approved this protocol on 17 May, 2004 (KOMC IRB 2004-01).

4. Statistics

For the crude analysis of baseline characteristics, we used independent t-test for continuous variables, and chi-square test for categorical variables.

To estimate the efficacy of ginseng on BP and hypertension-related symptom such as headache, we used paired t-test for the within-group effects and ANOVA test for the between-group effects.

The analysis was performed using SPSS for

Table 3. Comparison of Anti-hypertensive effect and the Improvement on VAS by Ginseng Species.

	Korean ginseng (n=64)	Chinese ginseng (n=58)	Red ginseng (n=33)	American ginseng (n=64)
Systolic BP, mmHg				
baseline	137.3 ± 10.2	136.8 ± 9.3	135.2 ± 9.0	136.5 ± 11.5
after 4 weeks	132.3 ± 15.6 ¹⁾	132.9 ± 14.4 ¹⁾	134.0 ± 13.2	134.4 ± 14.1
variance	-5.0 ± 16.1	-3.9 ± 14.8	-1.2 ± 11.3	-2.1 ± 12.5
Diastolic BP, mmHg				
baseline	86.7 ± 7.3	85.9 ± 6.5	86.6 ± 6.5	86.6 ± 6.5
after 4 weeks	80.6 ± 10.8 ²⁾	80.8 ± 9.2 ²⁾	85.3 ± 9.4	82.8 ± 10.1 ²⁾
variance	-6.1 ± 11.2	-5.1 ± 9.5	-1.3 ± 7.4	-3.8 ± 8.6
VAS on headache				
baseline	14.5 ± 26.9	9.0 ± 21.3	23.9 ± 30.2	15.2 ± 26.1
after 4 weeks	8.4 ± 19.8 ¹⁾	5.3 ± 15.4	13.0 ± 24.9 ²⁾	8.3 ± 19.3 ²⁾
variance	-6.0 ± 19.8	-3.6 ± 21.2	-10.9 ± 18.4	-6.9 ± 18.2

There was no significant difference among the groups by one-way ANOVA test
1), 2) : P < 0.05, P < 0.01 by paired t-test vs. baseline

Table 4. Comparison of Anti-hypertensive effect and the Improvement on VAS between Koreans and Chinese in Korean Ginseng-treated Group.

	Koreans (n=30)	Chinese (n=34)	Sig. ¹⁾
Systolic BP, mmHg			
baseline	133.4 ± 9.0	140.8 ± 10.2	0.003
after 4 weeks	131.1 ± 12.2	133.4 ± 18.2 †	N.S.
variance	-2.3 ± 11.1	-7.3 ± 19.4	N.S.
Diastolic BP, mmHg			
baseline	85.2 ± 8.2	89.0 ± 6.2	N.S.
after 4 weeks	83.2 ± 9.3	78.3 ± 11.7 ²⁾	N.S.
variance	-2.0 ± 9.4	-9.7 ± 11.6	0.005
VAS on headache			
baseline	22.3 ± 32.3	7.5 ± 18.8	N.S.
after 4 weeks	15.0 ± 26.0	2.7 ± 9.0	0.018
improvement	-7.3 ± 24.9	-4.9 ± 14.2	N.S.

1) Statistical significance was calculated by independent t-test

2) P<0.05 by paired t-test vs. baseline

Windows, version 10.0 (SPSS Inc., Chicago, Illinois, USA).

Results

1. Comparison of the Effectiveness of Ginseng according to Korean, Chinese, Red, and American Ginseng

There were 64 subjects treated with Korean ginseng, 58 treated with Chinese ginseng, 33

treated with red ginseng, and 64 treated with American ginseng. The baseline assessment did not differ among the groups (Table 2).

In the within-group analysis, Korean and Chinese ginseng reduced systolic and diastolic BP, and red ginseng reduced headache symptoms. American ginseng showed anti-hypertensive effect on diastolic BP and reduced headache symptoms. However, there was no statistical significance in the between-group analysis (Table 3).

Table 5. Comparison of Anti-hypertensive effect and the Improvement on VAS between Koreans and Chinese in Chinese Ginseng-treated Group.

	Koreans (n=28)	Chinese (n=30)	Sig. ¹⁾
Systolic BP, mmHg			
baseline	132.5 ± 9.8	140.8 ± 8.5	
after 4 weeks	130.6 ± 9.3	135.1 ± 17.9	N.S.
variance	-1.9 ± 9.2	-5.8 ± 18.6	N.S.
Diastolic BP, mmHg			
baseline	84.6 ± 7.6	87.2 ± 5.1	N.S.
after 4 weeks	83.8 ± 7.9	78.0 ± 9.7 ²⁾	0.017
variance	-0.9 ± 7.5	-9.1 ± 9.6	0.001
VAS on headache			
baseline	17.9 ± 28.1	0.7 ± 3.7	0.003
after 4 weeks	11.1 ± 20.8	0.0 ± 0.0 ²⁾	0.009
improvement	-6.8 ± 30.2	-0.6 ± 3.7	N.S.

1) Statistical significance was calculated by independent t-test

2) P<0.05 by paired t-test vs. baseline

Table 6. Comparison of Anti-hypertensive effect and the Improvement on VAS between Koreans and Chinese in American Ginseng-treated Group.

	Koreans (n=32)	Chinese (n=32)	Sig. ¹⁾
Systolic BP, mmHg			
baseline	134.5 ± 11.8	138.5 ± 11.1	N.S.
after 4 weeks	134.5 ± 12.7	134.3 ± 15.6	N.S.
variance	0.0 ± 10.0	-4.2 ± 14.4	N.S.
Diastolic BP, mmHg			
baseline	86.7 ± 7.4	86.6 ± 5.7	N.S.
after 4 weeks	85.7 ± 8.6	80.0 ± 10.7 ²⁾	0.022
variance	-1.0 ± 5.6	-6.6 ± 10.2	0.010
VAS on headache			
baseline	22.8 ± 30.0	7.5 ± 19.2	0.018
after 4 weeks	15.6 ± 24.9	0.9 ± 5.3	0.003
improvement	-7.2 ± 19.0	-6.6 ± 17.7	N.S.

1) Statistical significance was calculated by independent t-test

2) P<0.05 by paired t-test vs. baseline

2. Comparison of the Effectiveness of Ginseng between Koreans and Chinese

In the within-group analysis, Korean ginseng had no significant beneficial effect on Koreans, but it lowered systolic and diastolic BP in Chinese. Especially, in diastolic BP, there existed significant difference between the groups (Table 4).

Chinese ginseng had little effect on Koreans, but it lowered diastolic BP and headache symptoms in Chinese. There was a significant difference in anti-hypertensive effect on diastolic BP between Koreans and Chinese (Table 5).

American ginseng showed a similar effect with Chinese ginseng. It reduced diastolic BP

Table 7. Baseline Assessment according to the Type of Sasang Constitution

	Tae-eum (n=46)	So-yang (n=43)	So-eum (n=33)	Sig. ¹⁾
Age, yr	50.8 ± 8.8	52.3 ± 7.9	47.5 ± 7.8	N.S.
Sex (M/F)	28 / 18	19 / 24	15 / 18	N.S.
Medical history				N.S.
BP medication	12	10	10	N.S.
Diabetes	1	3	2	N.S.
Hyperlipidemia	4	4	5	N.S.
Systolic BP, mmHg	136.1 ± 9.5	133.3 ± 10.1	131.7 ± 8.5	N.S.
Diastolic BP, mmHg	87.7 ± 7.2	84.7 ± 8.3	84.5 ± 5.8	N.S.
VAS on headache	25.7 ± 32.2	18.8 ± 29.0	21.2 ± 30.0	N.S.
Ginseng type				
Korean ginseng	13	9	8	
Chinese ginseng	7	12	9	
Red ginseng	9	12	11	N.S.
American ginseng	17	10	5	

1) Statistical significance was calculated by one-way ANOVA test for continuous variables and chi-square test for categorical variables

Table 8. Comparison of Anti-hypertensive effect and the Improvement on VAS by the Type of Sasang Constitution.

	Tae-cum (n=46)	So-yang (n=43)	So-eum (n=33)	Sig. ¹⁾
Systolic BP, mmHg				
baseline	136.1 ± 9.5	133.3 ± 10.1	131.7 ± 8.5	N.S.
after 4 weeks	134.4 ± 13.1	131.5 ± 9.7	130.9 ± 12.3	N.S.
variance	-1.7 ± 11.0	-1.8 ± 9.4	-0.8 ± 10.6	N.S.
Diastolic BP, mmHg				
baseline	87.7 ± 7.2	84.7 ± 8.3	84.5 ± 5.8	N.S.
after 4 weeks	86.0 ± 9.1	83.7 ± 7.9	82.9 ± 9.0	N.S.
variance	-1.7 ± 8.2	-0.9 ± 7.5	-1.6 ± 6.2	N.S.
VAS on headache				
baseline	25.7 ± 32.2	18.8 ± 29.0	21.2 ± 30.0	N.S.
after 4 weeks	15.4 ± 25.8 ²⁾	12.8 ± 24.6 ²⁾	13.0 ± 21.6 ²⁾	N.S.
improvement	-10.2 ± 28.6	-6.0 ± 18.7	-8.2 ± 20.2	N.S.

1) Statistical significance was calculated by one-way ANOVA test

2) P<0.05 by paired t-test vs. baseline

significantly more in Chinese than in Koreans (Table 6).

3. Comparison of the Effectiveness and the Safety of Ginseng according to the Type of Sasang Constitution

The type of SCM was identified in Koreans. There were 46 subjects of *Tae-eum* type, 43 of *So-yang* type, and 33 of *So-eum* type. None of *Tae-yang* type were identified. In the between-group analysis, there was no significant difference in the subjects' baseline assessment (Table 7).

Systolic and diastolic BP were almost unchanged, but headache symptoms improved in all of the constitutional types (Table 8).

In safety assessment, there were no adverse effects or abnormal laboratory findings (Table 9).

Discussion

In this study, ginseng reduced subjects' BP. These results might be explained by the facts that it could reduce vascular resistance²⁷⁾, dilate lumen of vessels by inducing nitric oxide production in endothelial cells²⁶⁾, and inhibit intracellular calcium overload on erythrocytes membrane²⁹⁾. Especially, Korean and Chinese ginseng showed more positive effects. They reduced both systolic and diastolic BP significantly, while red ginseng had little effect on BP and American ginseng reduced only diastolic BP. These results could

Table 9. Comparison of the Change of Laboratory Findings and the Frequency of Adverse Effects by the Type of Sasang Constitution.

	Tae-eumin (n=46)	So-yangin (n=43)	So-eumin (n=33)	Sig. ¹⁾
Changes of				
AST, U/L	1.3 ± 4.8	0.5 ± 5.0	1.1 ± 7.8	N.S.
ALT, U/L	1.2 ± 14.3	-0.3 ± 6.9	0.3 ± 10.6	N.S.
BUN, mg/dL	-0.4 ± 4.2	-0.8 ± 3.2	-0.1 ± 2.4	N.S.
Cr, mg/dL	0.4 ± 2.5	0.0 ± 0.1	0.0 ± 0.1	N.S.
Adverse effects	0	0	0	N.S.

1) Statistical significance was calculated by one-way ANOVA test for the values of laboratory findings and chi-square test for the frequency of adverse effect

suggest that *Panax ginseng* is more useful for hypertension than *Panax Quinquefolium*, and is better as just dried raw material than after the steaming-and-drying process. However, it is not strong enough to confirm this suggestion, because there was no statistical significance in the between-subjects analysis by ANOVA.

The secondary analysis on the subjects' nationality revealed that all of the ginseng types showed more significant anti-hypertensive effect in Chinese than in Koreans. From these results, we could think that the physicians in China seemed to help the patients to have a more desirable life-style for controlling high BP, although all of the physicians involved in both nations were trained to adhere to the same protocol. It might be due to the fact that the Chinese physicians had to belabor the point, because most Chinese people were not used to clinical research. Furthermore, the Chinese physicians barely managed to collect enough volunteers because it is illegal to advertise for subjects in China. We also think that there still exists a possibility that a different genetic type caused the different efficacy of ginseng between Koreans and Chinese. However, previous reports, in which ginseng had the same efficacy on BP, pulse rate, and body temperature in Koreans and Chinese^{35,36}, don't support this possibility. As another consideration, ginseng is very expensive in China, so most of the subjects in China have not before had the opportunity of taking ginseng. It also might be regarded that the status of energy deficiency might be more prominent in Chinese than in Koreans.

In Korea, specialists of SCM recommend ginseng as a beneficial medicine helpful for recovering healthy status from energy deficiency especially for the So-eum type. When ginseng would be applied to the other types of SCM, they

insist that special attention should be paid to prevent adverse effects, because Yang, plentifully included in ginseng, could accelerate over-heat syndrome in the other constitutional types.

However, in this study, we did not observe any difference in anti-hypertensive effect among the *Sasang* types. Furthermore, there were no adverse effects in any of the subjects. Although these findings give rise to some controversy how accurate the determination of constitutional type was and whether the dose of ginseng used was enough, we think 4.5 g per day of ginseng should be safe regardless of constitutional type. In classical literature of herbal medicine, ginseng increases energy and body fluid, and relieves fatigue, thirst, mental and nervous exhaustion. It is possible that adverse effects could be reduced by ginseng's function of increasing body fluid.

In conclusion, we suggest *Panax ginseng* without any steam-drying process is more useful for high BP than other ginseng types, and all of the ginseng types used in this study are safe with the dosage of 4.5 g per day.

Conclusions

1. Korean and Chinese ginseng reduced systolic and diastolic BP, and red ginseng reduced headache symptoms. American ginseng showed anti-hypertensive effect on diastolic BP and reduced headache symptom. However, there was no statistical significance in the between-group analysis.

2. Korean ginseng had no significant beneficial effect on Koreans, but it lowered systolic and diastolic BP in Chinese. Especially, in diastolic BP, there existed significant difference between the groups ($p=0.005$).

3. Chinese ginseng had little effect on Koreans, but it lowered diastolic BP and headache symptoms in Chinese. There was a significant difference in anti-hypertensive effect on diastolic BP between Koreans and Chinese ($p=0.001$).

4. American ginseng showed a similar effect with Chinese ginseng. It reduced diastolic BP significantly more in Chinese than in Koreans ($p=0.010$).

5. In Koreans, there were 46 subjects of *Tae-eum* type, 43 of *So-yang* type, and 33 of *So-eum* type. In the between-group analysis, systolic and diastolic BP were almost unchanged, but headache symptoms improved in all of the constitutional types.

6. In safety assessment, there were no adverse effects or abnormal laboratory findings in any of the constitutional types.

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