J. Food Sci. Nutr.
Vol. 6, No. 1, p. 66~72 (2001)

Alteration of Lipid Metabolism by Ginseng Supplements with Different Levels of Vitamin E in High Cholesterol-Fed Rats

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Abstract

Ginseng may have antioxidant and pharmacologic effects similar to those of vitamin E. The interactive effect of ginseng and vitamin E was studied with respect to cholesterol metabolism and the antioxidant status. A ginseng supplement (0.1%, wt/wt) with comparable levels of vitamin E was provided with a high-cholesterol (1%, wt/wt) diet to rats for 5 weeks. The amount of vitamin E included in the ginseng-free and ginseng diets was either a low (low-E) or a normal (normal-E) level. The ginseng supplements significantly ($p<0.05$) altered the concentrations of plasma triglycerides in both the low-vitamin E group and normal-vitamin E group compared to the each ginseng-free group. The hepatic triglyceride and cholesterol contents were not significantly ($p>0.05$) different between groups regardless of the vitamin E level in the diet. The hepatic HMG-CoA reductase activity was significantly ($p<0.05$) lowered by the ginseng supplement in both the low-vitamin E and the normal-vitamin E groups compared to the ginseng-free group. The HMG-CoA reductase activity was also significantly ($p<0.05$) lowered with an increase of the dietary vitamin E in the ginseng-free group. The excretion of fecal neutral sterol was significantly ($p<0.05$) lower in the normal-E ginseng group than the low-E ginseng-free group. Neither dietary ginseng nor vitamin E significantly changed the hepatic antioxidant enzymes activity. This data indicates that ginseng supplements lower the concentration of plasma triglyceride and hepatic HMG-CoA reductase activity regardless of the dietary vitamin E level. This information may contribute to understanding the interactive effect of ginseng and vitamin E on cholesterol biosynthesis in high cholesterol-fed rats.

Key words: ginseng, vitamin E, HMG-CoA reductase, ACAT, fecal sterols, cholesterol metabolism, antioxidant enzymes

INTRODUCTION

Recently, the study and use of natural products in the treatment of a wide range of diseases, including heart disease, have gained considerable attention.

Ginseng, a well-known Korean traditional medicine, has a wide range of pharmacological and therapeutic actions. It acts on the central nervous system, cardiovascular system and endocrine secretion, promotes immune function and metabolism, possesses biomodulation action, anti-stress and anti-aging activities, and so on (1). Ginseng can also increase long-term resistance to stress and disease and therefore affects the lifespan (2).

Consumption of ginseng has been reported to contribute to a decreased risk of coronary heart disease since ginseng supplements lower the serum cholesterol and triglycerides in animals or humans (3,4). The plasma cholesterol concentration can be regulated by the biosynthesis of cholesterol, removal of cholesterol from the circulation, absorption of dietary cholesterol, and excretion of cholesterol via bile and feces. Cholesterol is essential for cell membranes, however, the unregulated accumulation of cholesterol causes atherosclerosis. Cellular cholesterol homeostasis is very important for the prevention of cardiovascular disease, and numerous studies have reported on the beneficial effects of HMG-CoA reductase and ACAT inhibitors on hypercholesteolemia and atherosclerosis (5,6). However, the effects of ginseng on cholesterol metabolism and the antioxidative status still require clarification.

Vitamin E is considered the first line of defense against lipid peroxidation in cell membranes. Accordingly, the present study investigated whether a ginseng supplement can exhibit vitamin E-like activity on cholesterol metabolism and antioxidant enzymes. The interactive effects of dietary ginseng and vitamin E were examined in high cholesterol-fed rats.

MATERIALS AND METHODS

Animals and diets

Forty male Sprague-Dawley weighing between 90 and 100 g were purchased from the Daehan Laboratory Animal Research Center Co. (Chungbuk, Korea). The animals were individually housed in stainless steel cages in a room with controlled temperature (24°C) and lighting (alternating 12-hour periods of light and dark). All the rats were fed a pellitized

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commercial chow diet for 6 days after arrival. Next the rats were randomly divided into four groups (n = 10) and fed a high cholesterol diet (1%, wt/wt) either with or without a ginseng (0.1%, wt/wt, Sigma Chemical Co.) supplement for 5 weeks. There were two level of vitamin E content in the ginseng and ginseng-free diets, a low (low-E) and a normal (normal-E) level. The composition of the experimental diet, as shown in Table 1, was based on the AIN-76 semisynthetic diet (7,8) and the low level of vitamin E used in the diet (5 IU/kg diet) included about a 20% marginal vitamin E level for growth (27 IU/kg diet) (9).

The animals were given food and distilled water *ad libitum* during the experimental period. The food consumption and weight gain were measured every day and every week, respectively. The feces collected during the last 3 days using metabolic cages was used for determining the fecal sterol. At the end of the experimental period, the rats were anesthetized with Ketamine following a 12-hour fast. Blood samples were taken from the inferior vena cava to determine the plasma lipid profile. The livers were removed and rinsed with physiological saline. All samples were stored at -70°C until analyzed.

Plasma and hepatic lipids

The plasma cholesterol concentration and HDL-cholesterol concentrations were determined using a commercial kit (Sigma) based on a modification of the cholesterol oxidase method of Allain et al. (10). The HDL-fractions were separated using a Sigma kit based on the heparin-manganese precipitation procedure (11). The plasma triglyceride concentrations were measured enzymatically using a kit from Sigma Chemical Co., a modification of the lipase-glycerol phosphate oxidase method (12). The hepatic lipids were extracted using the procedure developed by Folch et al. (13). The dried lipid residues were dissolved in 1 mL of ethanol for cholesterol and triglyceride assays. Triton X-100 and a sodium cholate solution (in distilled H_2O) were added to 200 μL of the dissolved lipid solution to produce final concentrations of 5 g/L and 3 mmol/L, respectively. The hepatic cholesterol and triglycerides were analyzed with the same enzymatic kit as used in the plasma analysis.

Table 1. Composition of experiment diets (%)

Groups	Ginseng-free		Ginseng	
	Low-E[4]	Normal-E[4]	Low-E	Normal-E
	n=10	n=10	n=10	n=10
Casein	20	20	20	20
D,L-methionine	0.3	0.3	0.3	0.3
Corn starch	15	15	15	15
Sucrose	49	49	48.9	48.9
Cellulose powder	5	5	5	5
Mineral mixture[1]	3.5	3.5	3.5	3.5
Low-E vitamin mixture[2]	1	-	1	-
Normal-E vitamin mixture[3]	-	1	-	1
Choline bitartrate	0.2	0.2	0.2	0.2
Corn oil	5	5	5	5
Cholesterol	1	1	1	1
Ginseng	-	-	0.1	0.1
Total	100	100	100	100

[1] AIN-76 mineral mixture
[2] Vitamin mixture with a low dietary vitamin E (in g/kg mixture): thiamin HCl, 0.6; riboflavin, 0.6; pyridoxine HCl, 0.7; niacin, 3.0; D-calcium pantothenate, 1.6; folic acid, 0.2; D-biotin, 0.02; cyanocobalamin (vitamin B_{12}), 0.001; retinyl palmitate premix, 0.8; DL-α-tocopherol, 0.455; vitamin D trituration, 0.25; menadium sodium bisulfide complex, 0.15; sucrose, finely powdered 991.624.
[3] AIN-76 vitamin mixture
[4] The vitamin E level in low-E and normal-E diets were 5 IU and 50 IU/kg diet, respectively.

HMG-CoA reductase and ACAT activities

Microsomes were prepared according to the method developed by Hulcher and Oleson (14) with a slight modification. Two grams of liver tissue were homogenized in 4 mL of an ice-cold buffer (pH 7.0) containing 0.1 M of triethanolamine, 0.02 M of EDTA, and 2 mM of dithiothreitol, pH 7.0. The homogenates were centrifuged for 10 min at 10,000 × g and then at 12,000 × g at 4°C. Next the supernatants were ultracentrifuged twice at 100,000 × g for 60 min at 4°C. The resulting microsomal pellets were then redissolved in 1 mL of a homogenation buffer for protein determination (15) and finally analyzed for HMG-CoA reductase and ACAT activities.

The HMG-CoA reductase activities were determined as described by Shapiro et al. (16) with a slight modification using freshly prepared hepatic microsomes. An incubation mixture (120 μL) containing microsomes (100 ~ 150 μg) and 500 nmol of NADPH (dissolved in a reaction buffer containing 0.1 M of tricthanolamine and 10 mM of EDTA) were preincubated at 37°C for 5 min. Next, 50 nmol of [^{14}C]-HMG-CoA (specific activity; 2.1420 GBq/mmol; NEM™ Life Science Products, Inc., Boston, MA) was added and the incubation was continued for 15 min at 37°C. The reaction was terminated by the addition 30 μL of 6 M of HCl and the resultant reaction mixture was incubated at 37°C for a further 15 min to convert the mevalonate into mevalonolactone. The incubation mixture was centrifuged at 10,000 × g for 5 min, and the supernatant was spotted on a Silica Gel 60 F_{254} TLC plate with a mevalonolactone standard. The plate was developed in benzene-acetone (1:1, V/V), and air-dried. Finally, the region Rf 0.3 ~ 0.6 region was removed by scraping using a clean razor blade and its ^{14}C radioactivity was determined using a liquid scintillation counter (Packard Tricarb 1600TR; Packard Instrument Company, Meriden, CT). The results were expressed as picomole mevalonate synthesized per min per mg protein.

The ACAT activities were determined using freshly prepared hepatic microsomes developed by Erickson et al. (17) as modified by Gillies et al. (18). To prepare the cholesterol substrate, 6 mg of cholesterol and 600 mg of Tyloxapol (Triton WR-1339, Sigma) were each dissolved in 6 mL of acetone, mixed well and completely dried in N_2 gas. The dried substrate was then redissolved in 20 mL of distilled water to a final concentration of 300 μg of cholesterol/mL. Next, reaction mixtures containing 20 μL of a cholesterol solution (6 μg

of cholesterol), 20 μL of a 1 M of potassium-phosphate buffer (pH 7.4), 5 μL of 0.6 mM bovine serum albumin, 50~100 μg of the microsomal fraction, and distilled water (up to 180 μL) were preincubated at 37°C for 30 min. The reaction was then initiated by adding 5 nmol of [^{14}C]-Oleoyl CoA (specific activity; 2.0202 GBq/mmol; NEM™ Life Science Products, Inc.) to a final volume of 200 μL; the reaction time was 30 min at 37°C. The reaction was stopped by the addition 500 μL of an isopropanol:heptane (4:1, v/v), 300 μL of heptane, and 200 μL of 0.1 M potassium phosphate (pH 7.4), then the reaction mixture was allowed to stand at room temperature for 2 min. Finally, an aliquot (200 μL) of the supernatant was subjected to scintillation counting. The ACAT activity was expressed as picomole of cholesteryl oleate synthesized per min per mg of microsomal protein.

Fecal sterols

The fecal neutral sterols were determined using a simplified micro-method developed by Czubayko et al. (19). A gas-liquid chromatography was carried out with a Hewlett-Packard gas chromatograph (Model 5809; Palo Alto, CA) equipped with a hydrogen flame-ionization detector and used a Sac™-5 capillary column (30 m×0.25 mm i.d., 0.25 μm film; Supelco Inc., Bellefonate, PA, USA). Helium was used as the carrier gas. The temperatures were set at 230°C for the column and 280°C for the injector/detector temperature. 5-α-cholestane (Supelco Inc.) was used as the internal standard. The daily neutral sterol excretion was calculated based on the amount of cholesterol, coprostanol and coprostanone in each sample. The fecal bile acid was extracted with t-butanol and quantified enzymatically with 3-α-hydroxysteroid dehydrogenase (20).

Plasma vitamin E concentration

The plasma α-tocopherol was determined according to the method of Bieri et al. (21). Two hundred microliters of plasma was added to 100 μL of tocopherol acetate (internal standard) and extracted by heptane. The collected heptane layer was then filtered using a syringe (0.5 M FH Membrane), dissolved in diethyl ether:methanol (1:3, v/v), and separated by HPLC. The chromatograph was equipped with a microBondapack C18 column and detected on UV 292 nm.

Antioxidant enzyme activities and TBARS concentration

The preparation of the enzyme source fraction in the liver tissue was as follows. One gram of liver tissue was homogenized in five-fold a 0.25 M of sucrose buffer, centrifuged at 600×g for 10 min to discard any cell debris, then the supernatant was centrifuged at 10,000×g for 20 min to remove the mitochondria pellet. Finally, the supernatant was further ultracentrifuged at 105,000×g for 60 min to obtain the cytosol supernatant. The amount of protein in the mitochondrial and cytosolic fractions was measured according to the method of Bradford (15) using bovine serum albumin as the standard.

The superoxide dismutase (SOD) activity was measured using Marklund and Marklund's (22) method with a slight modification. One hundred microliters of the cytosol supernatant was mixed with 1.5 mL of a Tris-EDTA-HCl buffer (pH 8.5), then 100 μL of 15 mM pyrogallol was added and the reaction mixture incubated at 25°C for 10 min. The reaction was terminated by adding 50 μL of 1 N HCl, then the activity was measured at 440 nm. One unit was determined as the amount of enzyme that inhibits the oxidation of pyrogallol by 50%. The activity was expressed as units/mg protein.

The catalase (CAT) activity was measured using Aebi's (23) method with a slight modification. The mitochondria pellet was dissolved in 1.0 mL of a 0.25 M of sucrose buffer. Ten microliters of the mitochondria solution was added to a cuvette containing 2.89 mL of a 50 mM potassium phosphate buffer (pH 7.4), and the reaction was initiated by adding 0.1 mL of 30 mM H_2O_2 to make a final volume of 3.0 mL at 25°C. The decomposition rate of H_2O_2 was measured at 240 nm for 5 min on a spectrophotometer. The molar extinction coefficient of 0.041 $mM^{-1}cm^{-1}$ was used to determine the CAT activity. The activity was defined as the μmole H_2O_2 decreased/mg protein/min.

The glutathione peroxidase (GSH-Px) activity was measured using Paglia and Valentine's (24) method with a slight modification. The reaction mixture contained 2.525 mL of a 0.1 M of Tris-HCl (pH 7.2) buffer, 75 μL of 30 mM glutathione, 100 μL of 6 mM NADPH, and 100 μL of glutathione reductase (0.24 unit). One hundred microliters of the cytosol supernatant was added to 2.8 mL of the reaction mixture and incubated at 25°C for 5 min. The reaction was initiated by adding 100 μL of 30 mM H_2O_2 and the absorbance was measured at 340 nm for 5 min. A molar extinction coefficient of 6.22×10^3 $M^{-1}cm^{-1}$ was used to determine the activity. The activity was expressed as the oxidized NADPH μmole/mg protein/min.

As a marker of lipid peroxidation production, the plasma TBARS (thiobarbituric acid reactive substances) concentration was measured using the method of Tarlardgis et al. (25). Briefly, 500 μL of plasma was well mixed with 3 mL of 5% trichloroacetic acid and 1 mL of freshly prepared 60 mM of thiobabituric acid (TBA). After incubation at 80°C for 90 min, the samples were cooled at room temperature and centrifuged at 1,000×g for 15 min, then the absorbance of the supernatant was measured at 535 nm using tetramethoxypropane (Sigma Chemical Co.) as the standard.

Statistical analysis

All data is presented as the mean±SE. The data was evaluated by one-way ANOVA using a SPSS (Statistical Package for Social Sciences, SPSS Inc., USA) software package program, and the differences between the means assessed using Duncans multiple-range test. Statistical significance was considered at $p<0.05$.

RESULTS

Food intake, weight gains, and organ weights

There was no significant difference in the food intake,

weight gain or organ weight between the various groups (Table 2). Accordingly, they were not seemingly affected by a ginseng or vitamin E supplement.

Plasma and hepatic lipids

The supplementation of 0.1% ginseng did not alter the plasma cholesterol concentration in either the low-E or normal-E groups compared to the control (ginseng-free) groups. However, there was a significant change in the plasma triglyceride concentration (Table 3). The plasma triglyceride concentration was significantly lowered in the ginseng-supplemented groups compared to the ginseng-free groups (1.16±0.05 mmol/L vs. 0.66±0.05 mmol/L in low-E group, 1.10±0.05 mmol/L vs. 0.63±0.05 mmol/L in normal-E group, mean±SE; $p<0.05$). The supplementation of ginseng with a normal level of vitamin E produced a significant increase in the plasma HDL-C/total-C ratio compared to the two low-E groups. The atherogenic index was significantly lower in the normal-E group than in the low-E group within ginseng-supplemented groups.

Hepatic HMG-CoA reductase and ACAT activities

The HMG-CoA reductase activity was significantly lowered by the ginseng supplement in both the low-E group (794.64±9.87 pmole/min/mg protein vs. 146.28±24.36 pmole/min/mg protein, mean±SE; $p<0.05$) and the normal-E group (358.82±11.4 pmole/min/mg protein vs. 140.92±17.02 pmole/min/mg protein) compared to all the ginseng-free groups (Fig. 1).

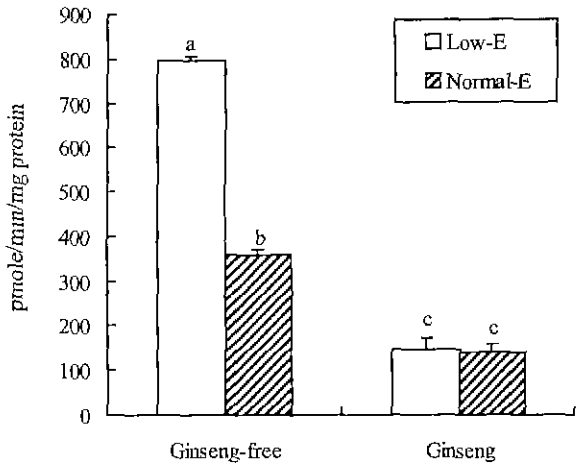

Fig. 1. Effect of ginseng and vitamin E supplementation on hepatic HMG-CoA reductase activities in high cholesterol-fed rats. Mean±S.E. The means not sharing a common letter are significantly different between groups ($p<0.05$).

This enzyme activity was also significantly lowered when the dietary vitamin E was changed from low-vitamin E to normal-vitamin E in the ginseng-free groups. Accordingly, the HMG-CoA reductase inhibitory effect was significantly enhanced by an increase in the dietary vitamin E level within the ginseng-free group. However, the hepatic ACAT activity was not dif-

Table 2. Effect of ginseng and vitamin E supplementation on food intakes, weight gains, and organ weights in high cholesterol-fed rats

Groups	Ginseng-free		Ginseng	
	Low-E	Normal-E	Low-E	Normal-E
Food intake (g/day)	19.44±0.44[1)NS]	20.66±0.42	19.89±0.32	19.58±0.06
Weight gains (g/week)	45.08±1.00[NS]	46.00±1.32	41.88±1.03	42.76±0.96
Organ weight (g)				
Liver	13.58±0.36[NS]	13.82±0.61	13.16±0.35	12.33±0.4
Heart	1.16±0.04[NS]	1.11±0.03	1.07±0.02	1.10±0.03
Kidney	2.45±0.04[NS]	2.32±0.07	2.29±0.05	2.30±0.07

[1)]Mean±S.E.
[NS]Not significantly different ($p<0.05$) between groups.

Table 3. Effect of ginseng and vitamin E supplementation on the plasma and hepatic lipids in high cholesterol-fed rats

Groups	Ginseng-free		Ginseng	
	Low-E	Normal-E	Low-E	Normal-E
Plasma				
Total-cholesterol (mmol/L)	3.83±0.25[1)a]	3.40±0.15[ab]	3.49±0.13[ab]	2.90±0.21[b]
HDL-cholesterol (mmol/L)	0.66±0.05[NS]	0.72±0.07	0.59±0.06	0.63±0.05
HDL-C/Total-C (%)	17.49±2.29[a]	20.78±2.35[ab]	17.12±1.66[a]	22.66±2.20[b]
Triglyceride (mmol/L)	1.16±0.07[a]	1.10±0.05[a]	0.66±0.05[b]	0.63±0.05[b]
Atherogenic index[2)]	4.80±0.62[ab]	3.75±0.43[ab]	5.35±0.61[a]	3.96±0.59[b]
Liver				
Cholesterol (mmol/g)	0.31±0.03[NS]	0.29±0.01	0.29±0.01	0.30±0.01
Triglyceride (mmol/g)	0.27±0.01[NS]	0.25±0.02	0.25±0.02	0.25±0.02

[1)]Mean±S.E.
[2)](Total cholesterol - HDL-cholesterol)/HDL-cholesterol
[NS]Not significantly different ($p<0.05$) between groups.
[ab]Means in the same row not sharing a common superscript are significantly different between groups ($p<0.05$).

ferent between groups (Fig. 2).

Fecal sterols

The daily excretion of fecal sterols is shown in Table 4. The effect of the ginseng supplementation resulted in some changes in the fecal neutral and total sterol under the cholesterol-fed conditions. The total neutral sterol was significantly lower in the normal-E ginseng group compared to the low-E ginseng-free group. Whereas the fecal acidic sterol was not significantly different between groups. The total fecal sterol excretion was significantly lower in the normal-E ginseng group than in the low-E ginseng-free group.

Concentrations of plasma vitamin E and TBARS, and activities of hepatic antioxidant enzymes

The plasma vitamin E concentration was significantly higher in those rats supplemented with normal-E than in the rats that received low-E ($p<0.05$) (Fig. 3). The ginseng supplement had no affect on the plasma vitamin E concentration.

No marked differences in the SOD, GSH-Px, and CAT activities and TBARS concentration were observed between the ginseng-free and ginseng-supplemented groups (Table 5). Therefore, the dietary vitamin E level did not appear to have any affect on these enzyme activities.

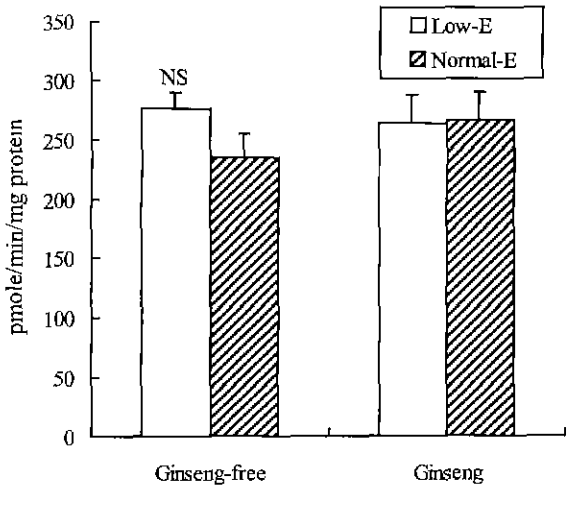

Fig. 2. Effect of ginseng and vitamin E supplementation on hepatic ACAT activities in high cholesterol-fed rats. Mean±S.E. ^{NS}Not significantly different ($p<0.05$) between groups.

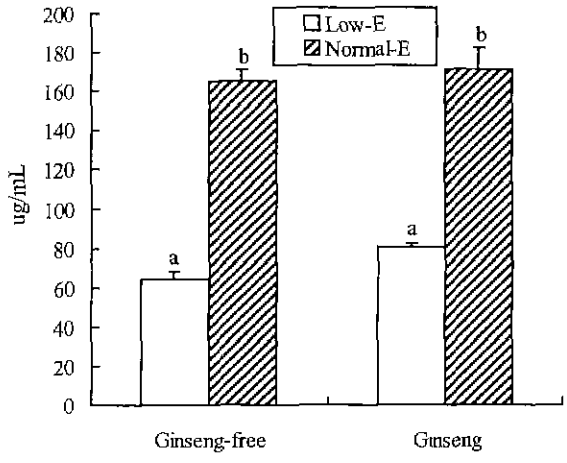

Fig. 3. Effect of ginseng and vitamin E supplementation on plasma vitamin E concentration in high cholesterol-fed rats. Mean±S.E. The means not sharing a common letter are significantly different between groups ($p<0.05$).

DISCUSSION

Ginseng is known to have an effect on hypolipidemia and increases resistance to coronary heart disease (26). Huong et al. (27) suggested that ginseng saponin, as well as vitamin E, had an inhibitory action on free radical-medicated lipid peroxidation. Accordingly, the combined effects of the ginseng and dietary vitamin E level were investigated to determine their possible interaction. The results suggest that the lipid-lowering effects of ginseng is evident by the changes in plasma triglyceride levels. The plasma triglyceride concentration was significantly lowered in the ginseng supplemented groups, however it was unaffected by dietary vitamin E.

The liver is the major site for the synthesis and net excretion of cholesterol, either directly as free cholesterol in the bile or after conversion into bile acid. Hepatic HMG-CoA reductase activity usually decreases under high-cholesterol feeding conditions using a negative feedback control (28). In this study, hepatic HMG-CoA reductase activity was lowered by a ginseng supplements.

Accordingly, the action of ginseng in the present study is similar to that of citrus bioflavonoids we have studied recently in high cholesterol-fed rats. It would appear that the lowering of HMG-CoA reductase, caused by the ginseng supplement, results in an increase in the absorption of dietary

Table 4. Effect of ginseng and vitamin E supplementation on fecal sterol concentration in high cholesterol-fed rats

Groups	Ginseng-free		Ginseng	
	Low-E	Normal-E	Low-E	Normal-E
Neutral sterol (mg/day)	400.30±13.19$^{1)a}$	334.14±33.75^{ab}	293.79±21.9^{ab}	239.49±28.43^{b}
Acidic sterol (mg/day)	1.84± 0.12^{NS}	1.60± 0.14	1.59±0.11	1.25± 0.12
Total fecal sterol (mg/day)	402.13±13.2^{a}	335.75±36.49^{ab}	295.36±23.1^{ab}	240.70±25.51^{b}

$^{1)}$Mean±S.E.
^{NS}Not significantly different ($p<0.05$) between groups.
^{ab}Means in the same row not sharing a common superscript are significantly different between groups ($p<0.05$).

Table 5. Effect of ginseng and vitamin E supplementation on hepatic activities SOD, CAT, GSH-Px and plasma TBARS concentration in high cholesterol-fed rats

Groups	Ginseng-free		Ginseng	
	Low-E	Normal-E	Low-E	Normal-E
SOD[1]	5.58±0.18[5]NS	5.55±0.22	5.36±0.19	5.33±0.14
CAT[2]	298.88±27.39NS	257.82±36.26	350.74±52.03	292.24±27.08
GSH-Px[3]	1.38±0.20NS	1.95±0.55	2.40±0.5	1.52±0.12
TBARS[4]	65.80±4.24NS	62.70±6.41	69.33±2.12	67.06±8.70

[1]Superoxide dismutase: unit/mg protein
[2]Catalase: decreased H_2O_2 μmole/mg protein/min
[3]Glutathione peroxidase: oxidized NADPH μmole/mg protein/min
[4]Thiobarbituric acid reactive substance: nmole/mL
[5]Mean±S.E.
NSNot significantly different ($p<0.05$) between groups.

cholesterol, thereby resulting in a decreased fecal sterol excretion.

Although many reports from clinical and experimental studies suggest that ginseng may have beneficial effects as an antiatherogenic agent by reducing elevated serum total cholesterol level and enhancing antioxidant status (29,30), our study revealed that ginseng has no significant potential. The dietary ginseng or vitamin E levels produced no affect on the antioxidant enzyme activities or plasma TBARS concentrations. The usual vitamin E requirement for most of the frequently used strains of rats is 27 IU/kg diet when the lipid comprises less than 10% of the diet (9). However, the low levels of vitamin E used in this study, a 5 IU/kg diet, seemed to maintain the antioxidant function and plasma TBARS concentration at a certain level for the given experimental period in high-cholesterol fed rats. There were no significant differences in the antioxidant enzyme activities or plasma TBARS concentration between the two vitamin E levels regardless of a ginseng supplement. In fact, the effect of dietary vitamin E on the antioxidant enzyme activities and serum lipid concentration appears to vary according to the species of experimental animal used. Recently, Sharma et al. (31) reported that vitamin E is a protective factor in atherosclerosis in rhesus monkeys, as a vitamin E injection decreased the concentrations of lipid peroxides and serum cholesterol and triglyceride in atherogenic diet-fed monkeys. In contrast, no marked changes in the SOD, GSH-Px, and CAT activities were observed in vitamin E-deficient rats (32), whereas a vitamin E-supplemented high cholesterol diet preserved the plasma SOD activity in rabbits (33).

The present study suggests that a ginseng supplement is effective in lowering the plasma triglyceride concentration and hepatic HMG-CoA reductase activities. However, it is also worth mentioning that the inhibitory effect on HMG-CoA reductase was greater with the normal vitamin E level than with the low vitamin E level in the ginseng-free group under high-cholesterol feeding conditions. This data would appear to indicate that the impact of a ginseng supplement is more beneficial than that of dietary vitamin E in improving the overall lipid metabolism.

ACKNOWLEDGEMENTS

This work was supported by a grant from the Ministry of Agriculture and Forestry of Korea.

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(Received August 24, 2000)