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Effects of ginseng on TNF-α, leptin and plasma lipid levels of rats fed a cholesterol-rich diet

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Abstract

This study assessed the effects of ginseng root powder on plasma total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride, leptin, and TNF-α levels of adult rats fed a cholesterol-rich diet. In this study, 48 healthy adult male Wistar Albino rats were divided into three groups: a control group (K), a cholesterol group (C), and a cholesterol+ginseng group (CG). The K group was fed a standard rat diet, whereas the C and CG groups were fed the same standard diet containing 5% cholesterol and 5% cholesterol+1 g/kg Panax ginseng root powder, respectively. Blood samples were taken on days 20 and 40 of the study. On days 20 and 40, the CG group had lower plasma total cholesterol levels than the C group ($p<0.05$). On day 20, there were no significant differences in plasma LDL-cholesterol levels between the CG and K groups. The reduction in plasma trygliceride levels (day 20), the increase in plasma HDL-cholesterol levels (day 20) and the decrease in plasma leptin levels (day 40) in the CG group compared to the C group were significant ($p<0.05$). However, there were no differences in TNF-α plasma levels on days 20 or 40 both between sampling times and among the groups. The results of this study support the use of ginseng to ameliorate abnormalities in serum lipid levels.

Keywords: Ginseng, cholesterol, leptin, adult rats, TNF-α.

INTRODUCTION

Food intake and body weight control are complex events regulated by neuropeptides released from the central nervous system (e.g., hypothalamus nuclei) and by peptides released from adipose tissue and gastrointestinal tract (35). Hyperlipidemia, obesity, diabetes, hypertension, and other cardiovascular diseases reduce life quality and contribute to high mortality rates (8, 37). Excessive dietary intakes of fats negatively affect blood parameters including plasma total lipids, total cholesterol, and triglycerides (14, 16). Increased adipose tissue leads to higher circulating leptin, adiponectin, and vaspin. Additionally, increased adipose tissue contributes to proinflammatory cytokines (18, 24, 35).

The negative effects that hypocholesterolemia, hyperlipidemia, obesity, hypertension and thrombosis have on human health have prompted the search for effective treatments and interventions. Pharmaceutical drug interventions (e.g., with statin, sibutramin, orlistat and phentermine) have considerable side effects. Therefore, herbal and botanical dietary supplements have been in demand (31). Ginseng is a herb with hypolipidemic, hypocholesterolemic, anti-obesity, anticarcinogenic, antihypertensive, antidiabetic, immunostimulatory and body fitness-enhancing effects (5, 20, 22, 25, 42). It has been reported that Panax ginseng increases HDL-cholesterol levels and reduces serum total cholesterol, triglyceride and LDL-cholesterol levels in humans (19) and rats (6, 16). In rats fed high fat diets, ginseng saponin applications reduce food consumption and body fat mass. Furthermore, ginseng saponin applications suppress serum leptin levels and hypothalamic neuropeptide Y (NPY) expression (18).

The objective of this study was to assess the effects of ginseng on the levels of tumor necrosis factor alpha (TNF-α), a proinflammatory cytokine, leptin, an adipose tissue indicator and serum lipids in rats fed a high cholesterol diet.

MATERIAL & METHOD

In this study, 48 healthy, adult male Wistar Albino rats were divided into three groups: a control group (K), a cholesterol group (C) and a

cholesterol+ginseng group (CG). The K group had ad libitum access to a standard rat diet (Purina) for 40 d. The C and CG groups had ad libitum access to the same diet containing 5% cholesterol (Sigma-Aldrich, Steinheim, Germany) and 5% cholesterol+1 g/kg Panax Ginseng root powder (General Nutrition Products (GNC), Inc., 1050 Woodruff Road Greenville, SC, USA), respectively, for 40 d. On days 20 and 40, blood samples were taken from 8 animals in each group. Total cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride levels were determined in an ILAB 300 autoanalyser using ILAB300 kits. TNF-α (Bendermed) and leptin (DRG) levels were determined using a commercial sandwich enzyme-linked immunosorbent assay (Bio-Tek Instruments, Inc). This study was approved by the Ethical Committee of the Faculty of Veterinary Medicine (Report No: 2012/001).

The data were analyzed with one-way ANOVA (SPSS 17). Statistical differences between sampling times and among the groups were tested by independent t-test and Duncan's multiple range test, respectively. Statistical significance was set at $p<0.05$.

RESULTS

Table 1. Effects of ginseng on total cholesterol, LDL-cholesterol, HDL-cholesterol, trygliceride, leptin and TNF-α levels in rats fed cholesterol-rich diet (Mean±SE, n=8).

	Control (K)		Cholesterol (C)		Cholesterol+ Ginseng(CG)	
	20th day	40th day	20th day	40th day	20th day	40th day
T.Cholesterol (mg/dl)	69,50±2,71^{C}	71,88±3,61^{c}	95,88±4,00^{A}	98,00±3,32^{a}	79,38±3,06^{B}	82,13±2,99^{b}
LDL (mg/dl)	20,25±1,31^{B}	21,13±1,09^{b}	29,50±2,82^{A}	30,50±1,38^{a}	24,25±1,83^{AB}	26,13±1,89^{a}
HDL (mg/dl)	24,38±1,45^{A}	24,50±2,03^{a}	15,38±1,24^{B}	18,38±1,25^{b}	22,88±2,42^{A}	21,13±2,11^{ab}
Trygliceride (mg/dl)	52,25±2,30^{C}	54,25±3,94^{b}	93,50±9,75^{A}	98,25±7,93^{a}	72,50±4,74^{B}	80,11±7,67^{a}
Leptin (ng/dl)	3,13±0,06	3,23±0,07^{b}	3,37±0,16^{y}	3,46±0,04^{xa}	3,29±0,09	3,12±0,04^{b}
TNF-α (pg/ml)	53,79±5,53	58,77±7,66	76,75±5,58	78,80±10,84	75,22±11,27	69,00±7,22

A,B,C: Different superscripts in the same line refers the differences among the groups in 20th day.
a, b, c: Different superscripts in the same line refers the differences among the groups in 40th day.
x, y: Different superscripts in the same line refers the differences between 20th and 40th day for each group ($p<0.05$).

DISCUSSION

On days 20 and 40, the plasma LDL-cholesterol levels were consistent with the plasma total cholesterol levels in K group, which is in accordance with other studies (6, 10, 26, 41, 42). The CG group had significantly lower and higher total cholesterol levels than the C and K groups ($p<0.05$, Table 1), respectively. Similar results have been reported in rats (6), humans (19) and mice (36). On day 20, there were no significant differences in LDL-cholesterol levels between the CG and K groups. Similar results have been reported in other studies (6, 26, 41, 42).

Ginseng enhances the ATP-binding cassette transporter G5 (ABCG5), ATP-binding cassette transporter G8 (ABCG8) and cholesterol 7α-hydroxylase (CYP7A1) expression, which are involved in the excretion of cholesterol into bile (9, 17). Ji and Gong (15) reported that LDLR (LDL-receptor) expression is upregulated by ginseng n-butanol extracts in rats, thereby reducting LDL-cholesterol and total cholesterol levels.

In this study, the increase in plasma triglyceride levels can be attributed to increasing LDL-cholesterol and VLDL-cholesterol levels (21, 29). Reduced HDL-cholesterol levels contribute to increased plasma triglyceride levels, which are associated with cardiovascular diseases and atherosclerosis (3, 7). On day 20, the CG group had lower plasma triglyceride levels than the C group ($p<0.05$, Table 1), which indicates that ginseng has hypolipidemic effects (13, 16, 19).

It has been reported that the activity of cholesterol ester transfer proteins (CETPs) increases in hyperlipidemic, hypertriglyceridemic, hyperlipidemic with hypercholesterolemia (28) and obese individuals (2). Furthemore, there is a negative correlation between CETP activity and HDL-cholesterol levels (2). While there is a positive correlation between HDL-cholesterol level and lipoprotein lipase (LPL) activity and a negative correlation between HDL-cholesterol and hepatic triglyceride lipase (HTGL), both HTGL and postheparin LPL activities are positively correlated with plasma total cholesterol and IDL triglyceride

levels (4). In this study, increased plasma LDL-cholesterol levels and reduced plasma HDL-cholesterol levels can be evaluated in terms of these enzyme activities.

Ji and Gong (15) reported that the effect of ginseng extracts on serum and hepatic triglyceride levels depends on the dose. Ginseng extracts reduce triglyceride levels by decreasing the expression of SREBP1-c genes involved in fatty acid synthesis (12) and by increasing LPL activity (15).

Leptin is produced by adipocytes; therefore, leptin levels in circulation are positively correlated with body fat mass (11, 27). On day 40, the plasma leptin levels of the CG group were significantly lower than those of the C group ($p<0.05$, Table 1), which agrees with the findings of Kim et al. (18), Lee et al. (23) and Yuan et al. (39). The reduction of leptin levels by ginseng saponin is attributed to a reduction in body fat mass and NPY expression (18). Song et al. (34) reported that ginseng extracts increases Lepr gen expression, which encodes the leptin receptors.

Mice (32, 33), rats (30) and humans (8, 40) fed high-fat diets have increased plasma leptin and TNF-α levels. Similarly, rats (1) and rabbits (38) fed aterogenic diets have increased plasma TNF-α, total cholesterol and triglyceride levels. Depending on the Panax notoginseng saponin application, the reduction in TNF-α level is simulatenous with a reduction in plasma lipids (38). However, Joo et al. (16) reported that while Panax notoginseng extracts significantly decreased triglyceride and LDL-cholesterol levels in rats, they had no effect on TNF-α level. In condusion, it is thought that ginseng has hypolipidemic effects and that these results contribute to the existing literature.

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REFERENCES

1. Ahmed HH, Abdalla MS, Eskander EF, Al-khadragy, Massoud MN. Hypolipidemic influence of sargassum subrepandum, mechanism of action. European Review for Medical and Pharmacological Sciences, 2012; 16(3): 112-120.
2. Arai T, Yamashita S, Hirano K, Sakai N, Kotani K, Fujioka S. Increased plasma cholesteryl ester transfer protein in obese subjects a possible mechanism for the reduction of serum HDL cholesterol levels in obesity. Arterioscler Thromb, 1994; 14: 1129-1136.
3. Ballantyne CM, Olsson AG, Cook TJ, Mercuri MF, Pedersen TR, Kjekshus J. Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4s. Circulation, 2001; 104: 3046-3051.
4. Blades B, Vega GL, Grundy SM. Activities of lipoprotein lipase and hepatic triglyceride lipase in postheparin plasma of patients with low concentrations of hdl cholesterol. Arteriosclerosis and Thrombosis, 1993; 13: 1227-1235.
5. Chung SH, Choi CG, Park SH. Comparisons between white ginseng radix and rootlet for antidiabetic activity and mechanism in KKAy mice. Arch Pharm Res, 2001; 24: 214-218.
6. Cicero AFG, Vitale G, Savino G, Arletti R. Panax notoginseng (Burk.) effects on fibrinogen and lipid plasma level in rats fed on a high-fat diet. Phytother Res, 2003; 17: 174-178.
7. Fauvel J, Bonnet E, Ruidavets JB, FerrieÁres J, Toffoletti A, Massip P. An interaction between apo C-III variants and protease inhibitors contributes to high triglyceride/low HDL levels in treated HIV patients. AIDS, 2001; 15: 2397-2406.
8. Gerenli M, Tuğrul A, Demir M, Arıkan E, Güldiken S, Azcan Ş. The relationship between proinflammatory cytokine levels and fibrinolytic system in obese patients. Trakya Univ Tip Fak Derg, 2008; 25(1): 44-51.
9. Graf GA, Li WP, Gerard RD, Ingrid G, White A, Cohen JC, Hobbs HH. Coexpression of ATP-binding cassette proteins ABCG5 and ABCG8 permits their transport to the apical surface. Journal of Clinical Investigation, 2002; 110: 659-669.
10. Harini M, Astirin OP. Blood cholesterol levels of hypercholesterolemic rat (rattus norvegicus) after VCO treatment. Bioscience, 2009; 1(2): 53-58.
11. Havel PJ. Role of adipose tissue in body-weight regulation: Mechanisms regulating leptin production and energy balance. Proc Nutr Soc, 2000; 59: 359-371.
12. Horton JD, Goldstein JL, Brown MS. SREBPs, activators of the complete program of cholesterol and fatty acid synthesis in the liver. Journal of Clinical Investigation, 2002; 109: 1125-1131.
13. Inoue M, Wu CZ, Dou DQ, Chen YJ, Ogihara Y. Lipoprotein lipase activation by red ginseng saponins in hyperlipidemia model animals. Phytomedicine, 1999; 6(4): 257-265.
14. Ismail MF, Gad MZ, Hamdy MA. Study of hypolipidemic properties of pectin garlic and ginseng in hypercholesterolemic rabbits. Pharmacological Research, 1999; 39(2): 157-165.
15. Ji W, Gong BQ. Hypolipidemic effects and mechanisms of Panax notoginseng on lipid profile in hyperlipidemic rats. Journal of Ethnopharmacology, 2007; 113: 318-324.
16. Joo IIW, Ryu JH, Oh HJ. The influence of sam-chil-geun (panax notoginseng) on the serum lipid levels and inflammations of rats with hyperlipidemia induced by poloxamer-407. Yonsei Med J, 2010; 51(4): 504-510.
17. Kawase A, Yamada A, Gamou Y, Tahara C, Takeshita F, Murata K. Increased effects of ginsenosides on the expression of cholesterol 7a-hydroxylase but not the bile salt export pump are involved in cholesterol metabolism. J Nat Med, 2013; 67: 545-553.

18. Kim JH, Hahm DH, Yang DC, Kim JH, Lee HJ, Shim I. Effect of crude saponin of korean red ginseng on high-fat diet-ınduced obesity in the rat. J Pharmacol Sci, 2005; 97(1): 124-131.

19. Kim SH, Park KS. Effects of panax ginseng extract on lipid metabolism in humans. Pharm Res, 2003; 48: 511-513.

20. Kim YR, Lee SY, Shin BA, Kim KM. Panax ginseng blocks morphine-induced thymic apoptosis by lowering plasma corticosterone level. Gen Pharmacol, 1999; 32: 647-652.

21. Kissebah AH, Alfarsi S, Evans DJ, Adams PW. Integrated regulation of very low density lipoprotein triglyceride and apolipoprotein-B kinetics in non-insulin-dependent diabetes mellitus. Diabetes, 1982; 31: 217-225.

22. Lee DCW, Lau ASY. Effects of panax ginseng on tumor necrosis factor- α -mediated inflammation: a mini-review. Molecules, 2011; 16: 2802-2816.

23. Lee YS, Cha BY, Yamaguchi K, Choi SS, Yonezawa T, Teruya T. Effects of Korean white ginseng extracts on obesity in highfat diet-induced obese mice. Cytotechnology, 2010; 62: 367-376.

24. Li Q, Chen R, Moriya J, Yamakawa J, Sumino H, Kanda T, Takahashi T. Novel adipocytokine, visceral adipose tissue-derived serine protease Inhibitor (vaspin) and obesity. The Journal of International Medical Researc, 2008; 36: 625-629.

25. Liu CX, Xiao PG. Recent advances on ginseng research in China. J Ethnopharmacol, 1992; 36: 27-38.

26. Liu R, Zhang JZ, Liu WC, Kimura Y, Zheng YN. Anti-obesity effects of protopanaxdiol types of ginsenosides isolated from the leaves of American ginseng (panax quinquefolius L.) in mice fed with a high-fat diet. Fitoterapia, 2010; 81: 1079-1087.

27. Maffei M, Halas J, Ravussin E, Pratley RE, Lee GH, Zhang Y. Leptin levels in human and rodent: Measurement of plasma leptin and ob RNA in obese and weight-reduced subjects. Nat Med, 1995; 1:1155-1161.

28. McPherson R, Mann CJ, Tall AR, Hogue M, Martin L, Milne RW, Marcel YL. Plasma concentrations of cholesteryl ester transfer protein in hyperlipoproteinemia: Relation to cholesteryl ester transfer protein activity and other lipoprotein variables. Arterioscler Thromb, 1991; 11: 797-804.

29. Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN. Triglycerides and cardiovascular disease a scientific statement from the American heart association. Circulation, 2011; 123: 2292-2333.

30. Mohamed MM. Effects of chitosan and wheat bran on seruml, TNF- α, lipid profile and oxidative status in animal model of non-alcoholic fatty liver. Aust J Bas Appl Sci, 2011; 5(10): 1478-1488.

31. Padwal RS, Majumdar SR. Drug treatments for obesity: orlistat, sibutramine and rimonabant. Lancet, 2007; 369(9555): 71-77.

32. Park NY, Rico CW, Lee SC, Kang MY. Comparative effects of doenjang prepared from soybean and brown rice on the body weight and lipid metabolism in high fat-fed mice. J Clin Biochem Nutr, 2012; 51(3): 235-240.

33. Silha JV, Weiler HA, Murphy LJ. Plasma adipokines and body composition in response to modest dietary manipulations in the mouse. Obesity (Silver Spring), 2006; 14: 1320-1329.

34. Song YB, An YR, Kim SJ, Park HW, Jung JW, Kyung JS. Lipid metabolic effect of Korean red ginseng extract in mice fed on a high-fat diet. J Sci Food Agric, 2012; 92: 388-396.

35. Stanley S, Wynne K, Mcgowan B, Bloom S. Hormonal regulation of food ıntake. Physiol Rev, 2005; 85: 1131-1158.

36. Wan JB, Lee SMY, Wang JD, Wang N, He CW, Wang YT, Kang JX. Panax notoginseng reduces atherosclerotic lesions in ApoE-deficient mice and inhibits TNF- α -induced endothelial adhesion molecule expression and monocyte adhesion. J Agric Food Chem, 2009; 57(15): 6692-6697.

37. Xiong Y, Shen L, Liu KJ, Tso P, Xiong Y, Wang G, Woods SC, Liu M. Antiobesity and antihyperglycemic effects of ginsenoside rb1 in rats. Diabetes, 2010; 59 (10): 2505-2512.

38. Yi J, Xiaohui L, Ya L, Haigang Z. Atherosclerosis lesion is accelerated by persistent systemic inflammation but attenuated by saponins from Panax Notoginseng in rabbits. J Med Col PLA, 2008; 23: 38-44.

39. Yuan HD, Kim SJ, Quan HY, Huang B, Chung SH. Ginseng leaf extract prevents high fat diet-ınduced hyperglycemia and hyperlipidemia through ampk activation. J Ginseng Res, 2010; 34(4): 369-375.

40. Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. Creactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol, 1999; 19: 972-978.

41. Yun SN, Ko SK, Lee KH, Chung SH. Vinegar-processed ginseng radix ımproves metabolic syndrome ınduced by a high fat diet in ICR mice. Arch Pharm Res, 2007; 30(5): 587-595.

42. Yun SN, Moon SJ, Ko SK, Im BO, Chung SH. Wild ginseng prevents the onset of high-fat diet ınduced hyperglycemia and obesity in ICR mice. Arch Pharm Res, 2004; 27(7): 790-796.