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 triglyceride 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, triglyceride, leptin and TNF-α levels in rats fed cholesterol-rich diet (Mean±SE, n=8).

<table>
<thead>
<tr>
<th></th>
<th>Control (K)</th>
<th>Cholesterol (C)</th>
<th>Cholesterol+Ginseng(CG)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20th day</td>
<td>40th day</td>
<td>20th day</td>
</tr>
<tr>
<td>T.Cholsterol (mg/dl)</td>
<td>69,50±2,71c</td>
<td>71,88±3,61c</td>
<td>95,88±4,00a</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>20,25±1,31h</td>
<td>21,13±1,09h</td>
<td>29,50±2,82h</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>24,38±1,45a</td>
<td>24,50±2,03a</td>
<td>15,38±1,24a</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>52,25±2,30c</td>
<td>54,25±3,94b</td>
<td>93,50±9,75b</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>3,13±0,06a</td>
<td>3,23±0,07b</td>
<td>3,37±0,16c</td>
</tr>
<tr>
<td>TFN-α (ng/ml)</td>
<td>53,79±5,53</td>
<td>58,77±7,66</td>
<td>76,75±5,58</td>
</tr>
</tbody>
</table>

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 reducing 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). Furthermore, there is a negative correlation between CETP activity and HDL-cholesterol levels (2). While there is a positive correlation between CETP and hepatic triglyceride lipase (HTGL), both HTGL and postheparin LPL activities are positively correlated with plasma total cholesterol and IDL triglyceride levels.
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 atherogenic 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 conclusion, it is thought that ginseng has hypolipidemic effects and that these results contribute to the existing literature.

Acknowledgements

This study was supported by The Scientific Research Projects Coordination Unit of Selcuk University (Project number: 12102002). None of the authors of this paper has a financial or personal relationship with other people or commercial identity mentioned in our paper that might lead to a conflict of interest for any of the authors.

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