Effects of Subchronic Panax Ginseng Administration Against TCDD-Induced Hypercholesterolemia In Rats

Yong-Kweon Cho[1], Ja-Young Moon[1], Hyung-Ok Sohn[2], Hak-Cheol Hyun[2], Dong-Wook Lee[2], Chul-Won Lee[1], Dae-Ook Kang[1], Kwon-Chul Ha[1]

[1]Changwon National University
[2]KT&G Central Research Institute

Introduction

2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) is the most potent member of a large family of dioxin-like compounds that are ubiquitous environmental contaminants. The lipophilic nature of TCDD causes the compound to be stored in the liver, adipose tissue and breast milk. TCDD has been reported to be one of the most toxic molecules, causing acute and chronic toxicity, including chloracne, thymic atrophy and immunotoxicity, wasting syndrome, hepatotoxicity, teratogenicity and hypercholesterolemia in animals[1-3].

Korean ginseng (*Panax ginseng* C.A. Meyer) is one of the most widely used medicinal plants, particularly in traditional oriental medicine. It has a wide range of pharmacological and physiological actions. Pharmacological effects of ginseng have been demonstrated in the CNS and in cardiovascular, endocrine, and immune systems. Many reports from clinical and experimental studies suggested that ginseng may have beneficial effects as an anti-hyperlipidemic agent on reducing serum total cholesterol level[4,5]. In this study, to achieve a better understanding of subchronic effects of water extracts of *Panax* ginseng against TCDD-induced hypercholesterolemia, we analyzed serum biochemical changes in rats after single administration of TCDD and/or subchronic administration of *Panax* ginseng extracts.

Materials and Methods

For this study, 120 male S.D rats (8 weeks old, 190-210 g bw) were divided into four groups: Control group, TCDD administered group, ginseng extracts administered group, co-administered group with TCDD and ginseng extracts. After being acclimatized for 1 week, the TCDD-administered group was given a single intraperitoneal dose of 25 mg TCDD/kg bw. The ginseng extracts-administered group received intraperitoneally 100 mg/kg/every other day for 1 month. For co-administered group with TCDD and ginseng extracts, *Panax* ginseng extracts were intraperitoneally administered to rats at 100 mg/kg/every other day (0.5 ml/kg bw) for 1 month after single intraperitoneal dose of 25 mg of TCDD/kg bw. The control group received the same amount of physiological saline every other day for 1 month. Ten milliliters of blood was collected at day 1, 2, 5, 16 and day 32 following exposure to TCDD for the analysis of serum biochemical parameters. Serum samples (5/dose/time point) were analyzed on an Automatic Chemistry Analyzer (Hitachi Model 7020, Japan) using commercially available reagents from Roche Diagnostics (GmbH, Mannheim, Germany). Determined endpoints consisted of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, low density lipoprotein (LDL)-cholesterol, high density lipoprotein (HDL)-cholesterol, and triglyceride (TG).

Results and Discussion

Panax ginseng extracts were intraperitoneally administered to male S.D rats at 100 mg/kg/every other day for 1-month period after single intraperitoneal dose of 25 mg TCDD/kg bw. As both TCDD and ginseng extracts modulate liver function, serum enzymes indicative of hepatotoxicity were measured. Treatment with TCDD alone at 25 mg/kg bw increased serum enzyme activity of ALT and AST at 32 days with statistical significance, indicating that liver damage occurred maximally at that time (Fig. 1). Ginseng extract alone caused insignificant changes in serum ALT, while it caused a gradual decrease in AST as the exposure time increased. Co-administration of TCDD and ginseng extracts caused statistically significant decrease in serum ALT and AST activities at 16 days and/or 32 days after exposure to TCDD towards the normal value of the control (Fig. **1**). These results suggest that *Panax* ginseng extracts possess a protective action against TCDD-induced hepatotoxicity.

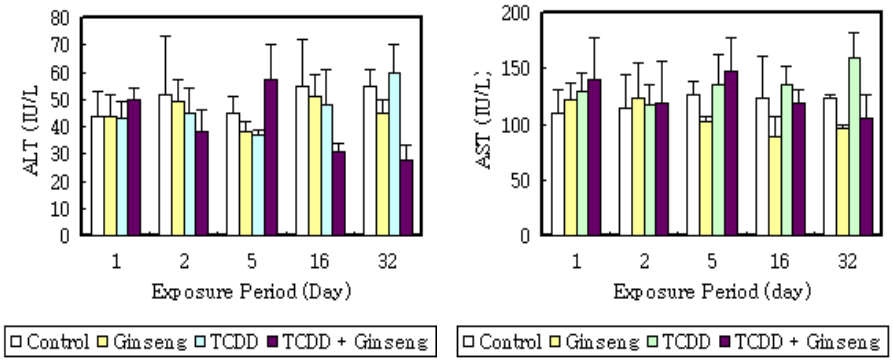

Fig. 1. Effect of TCDD and/or Ginseng extracts on serum ALT (A) and AST (B) in rats.

The serum levels of HDL-cholesterol, LDL-cholesterol, total cholesterol, and triglycerides were measured in blood samples from rats exposed to TCDD and/or ginseng extracts as described in Materials and Methods. As shown in Fig. 2, TCDD at 25 mg/kg bw significantly increased serum HDL-cholesterol concentrations at all time points. Ginseng extracts also increased serum HDL-cholesterol concentrations at 16 and 32 days, but the increase was not significant. In rats co-administered TCDD and ginseng extracts, significantly increased serum HDL-cholesterol level was observed at 5 days after exposure compared to that administered either TCDD or ginseng extracts. However, after 5 days, the serum HDL-cholesterol level decreased. At 32 days, the serum HDL-cholesterol level was much lower than that of control group. To understand the dual effect of ginseng extracts on the serum HDL-cholesterol, further studies are necessary.

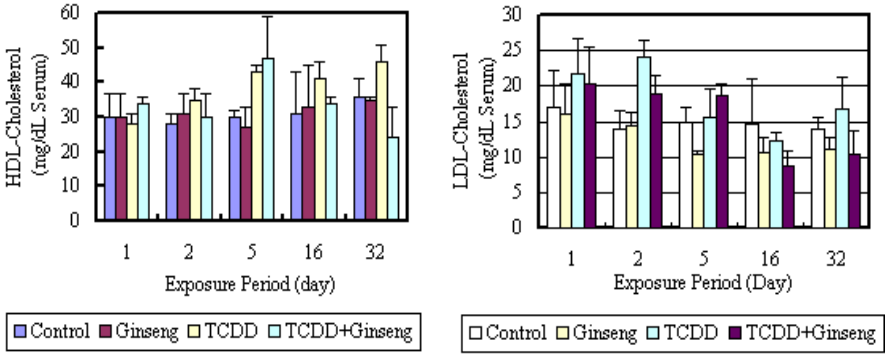

Fig. 2. Serum HDL- and LDL-cholesterol concentrations in rats treated with single i.p injection of 25 mg TCDD/kg bw and/or 100 mg Ginseng extracts/kg bw.

TCDD at 25 mg/kg bw increased serum total cholesterol concentrations at all time points (Fig. 3). In contrast, progressive decrease in serum total cholesterol concentrations was observed through whole experimental period following exposure to ginseng extracts, suggesting that ginseng extracts decrease dose- and exposure time-dependently the level of serum total cholesterol. Ginseng extracts remarkably decreased serum total cholesterol concentrations increased by TCDD exposure towards the normal value of the control. Serum triglyceride levels were dramatically increased by TCDD exposure at 1 day and 2 days following exposure to 25 mg TCDD/kg body weight.

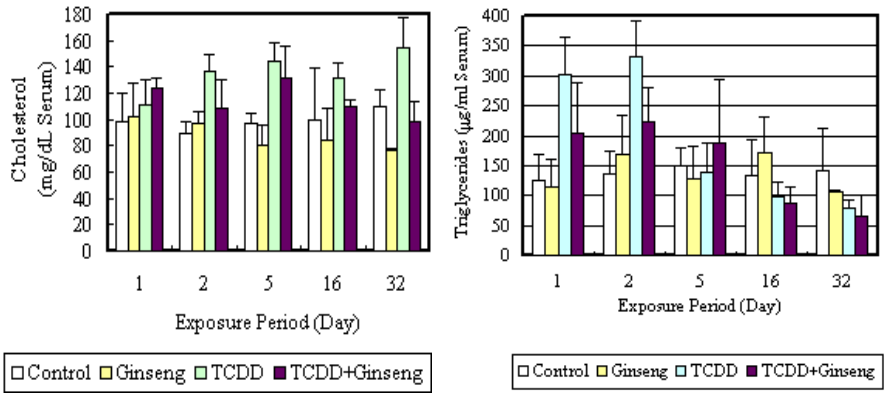

Fig. 3. Serum total cholesterol and triglycerides concentrations in rats treated with single i.p injection of 25 mg TCDD/kg bw and/or 100 mg Ginseng extracts/kg bw.

Acknowledgments
This work was supported by grant from Korea Research Foundation (KRF2003-005-I00075).

References

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