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Review

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Effects of Intake of Soy and Non-Soy Legume on Serum HDL-Cholesterol Levels

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Abstract

High-density lipoprotein (HDL) has been shown to have a variety of functions that contribute to anti-atherogenesis. Here we review meta-analyses on the effects of intake of soy protein and isoflavones on serum HDL-cholesterol (HDL-C) levels, and we would also review meta-analysis on the effects of intake of non-soy legume on serum HDL-C, to make "Dietary Reference Intake for Japanese 2020". We searched meta-analyses of randomized, placebo-controlled trials. A search was conducted by using PubMed, Embase and Google Scholar, with the following keywords: soy and HDL and meta-analysis. The search period was comprised from 2007 up to July 2018. We found three meta-analyses about effects of intake of soy protein and isoflavones on HDL-C after 2007. All meta-analyses reported that intake of soy protein and isoflavones was associated with a significant increase of HDL-C. We found the meta-analysis which evaluated effects of intake of non-soy legume on HDL-C, in which a significant association of intake of non-soy legume with HDL-C was not obtained due to a significant heterogeneity of collected data. In conclusion, intake of soy was significantly associated with elevation of HDL-C; however, non-soy consumption was not associated with a significant increase of HDL.

Keywords: High-density lipoprotein; Isoflavones; Non-soy legume; Soy protein

Introduction

High-density lipoprotein (HDL) has been shown to have a variety of functions that contribute to anti-atherogenesis: reverse cholesterol transport from the peripheral tissues to liver, promotion of macrophage cholesterol efflux, anti-inflammatory and anti-oxidative effects [1-3]. Therefore, low HDL-cholesterol (HDL-C) level is significantly associated with the development of coronary artery diseases (CADs) [4, 5].

Soy protein and isoflavones have been proposed to reduce the risk of CAD.

We previously studied effects of intake of soy protein and isoflavones on serum HDL-C levels to make "Dietary Reference Intakes for Japanese 2015", by using data obtained by clinical trials which evaluated effects of intake of soy protein and isoflavones on HDL-C in Asian populations, and data obtained from meta-analyses [6]. In the analysis of randomized, placebo-controlled trials (RCTs) to evaluate effects of soy protein and isoflavones on HDL-C which were performed in Asian populations, three RCTs denied a significant effect of intake of soy protein and isoflavones on serum HDL-C [7-9]. However, in two RCTs which investigated the effects of combination of isoflavones intake and walking, serum HDL-C significantly increased [10, 11]. The meta-analyses performed before 2007 showed a beneficial effect of intake of soy protein and isoflavones on serum HDL-C [12-15].

Here we review meta-analyses on the effects of intake of soy protein and isoflavones on serum HDL-C levels, and we would also review meta-analysis on the effects of intake of non-soy legume on serum HDL-C, to make "Dietary Reference Intake for Japanese 2020".

Materials and Methods

To make "Dietary Reference Intake for Japanese 2020", we searched meta-analyses of RCTs. A search was conducted by using PubMed, Embase and Google Scholar, with the following keywords: soy and HDL and meta-analysis. The search period was comprised from 2007 up to July 2018.

Results

Meta-analyses evaluated effects of intake of soy protein and isoflavones on HDL-C were shown in Table 1.

We found three meta-analyses about effects of intake of soy protein and isoflavones on HDL-C after 2007 [16-18]. All meta-analyses reported that intake of soy protein and isoflavones was associated with a significant increase of HDL-C.

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Table 1. Meta-Analyses Evaluated Effects of Intake of Soy Protein and Isoflavones on HDL-C

Authors	Assessed studies	Subjects studied	Effects on HDL-C	Effects on other lipids and glucose metabolism
Tokede et al [16]	RCTs assessing the effects of soy on the lipid profile	35 studies were included. Treatment duration ranged from 4 weeks to 1 year	There was a significant increase in serum HDL-C, 1.40 (95% CI: 0.58 - 2.23) mg/dL	Intake of soy products resulted in a significant reduction in serum LDL-C, -4.83 (95% CI: -7.34 to -2.31) mg/dL, TG, -4.92 (95% CI: -7.79 to -2.04) mg/dL, and TC, -5.33 (95% CI: -8.35 to -2.30) mg/dL
Yang et al [17]	RCTs were included in which soy products supplementation was the only intervention in subjects with type 2 diabetes	Eight studies were included according to the criteria	The intake of soy products was associated with a significant increase in HDL-C (0.05 mmol/L; 95% CI: 0.04 - 0.06)	The intake of soy products was associated with a significant reduction in TC (by 0.42 mmol/L; 95% CI: -0.70 to -0.14), TG (by 0.22 mmol/L; 95% CI: -0.38 to -0.07) and LDL-C (by 0.30 mmol/L; 95% CI: -0.60 to -0.00). There were no significant effects on fasting glucose, insulin and glycated hemoglobin
Anderson et al [18]	RCTs related to soy protein intake and serum lipoprotein changes	Analyses included 20 parallel-design studies and 23 crossover studies	In parallel studies, net serum HDL-C values were 3.2% higher ($P < 0.007$) with soy versus control	Soy protein intake was associated with net changes in LDL-C values of -0.23 mmol/L (95% CI: -0.28 to -0.18 mmol/L) or a 5.5% reduction in parallel studies and -0.16 mmol/L (95% CI: -0.22 to -0.11 mmol/L) or a reduction of 4.2% with crossover studies ($P < 0.001$ for parallel versus crossover). In parallel studies, TG values were 10.7% lower ($P < 0.008$) for soy versus control

CI: confidence interval; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density-cholesterol; RCT: randomized controlled trial; TC: total cholesterol; TG: triglyceride.

We found the meta-analysis which evaluated effects of intake of non-soy legume on HDL-C (Table 2) [19]. Intake of non-soy legume was significantly associated with reduction in total cholesterol (TC) and low-density lipoprotein (LDL)-C; however, a significant association of non-soy legume consumption with HDL-C was not obtained due to a significant heterogeneity of collected data.

Discussion

In our previous study, all meta-analyses suggested that intake of soy protein and isoflavones was significantly associated with elevation of HDL-C [6]. In the present study using meta-analyses published after 2007, we found three studies [16-18].

In the study by Tokede et al, 35 studies were included in their analyses [16]. Treatment duration ranged from 4 weeks to 1 year. Intake of soy products resulted in a significant increase in serum HDL-C, 1.40 (95% CI: 0.58 - 2.23) mg/dl, in addition to a significant reduction in serum LDL-C, triglyceride (TG) and TC [16].

Yang et al systematically reviewed the effects of soy products consumption on serum lipid profiles and glycemic control in patients with type 2 diabetes [17]. Eight studies were included according to the criteria. Intake of soy products was associated with a significant increase in HDL-C, in addition to a significant reduction in TC, TG and LDL-C [17]. However, there were no significant effects on fasting glucose, insulin and glycated hemoglobin.

In the study by Anderson et al, RCTs were assessed that met these requirements: soy protein intake compared with non-soy protein, provided information on serum LDL-C, provided no more than 65 g of soy protein daily, and obtained LDL-C measurements between 4 and 18 weeks of treatment [18]. Analyses included 20 parallel-design studies and 23 crossover studies. In parallel studies, net serum HDL-C values were

Table 2. Meta-Analysis Evaluated Effects of Intake of Non-Soy Legume on HDL-C

Authors	Assessed studies	Subjects studied	Effects on HDL-C	Effects on other lipids
Bazzano et al [19]	RCTs which were selected which compared a non-soy legume diet to control, had a minimum duration of 3 weeks, and reported blood lipid changes during intervention and control	10 RCTs	The pooled mean net change in HDL-C was 0.85 mg/dL (95% CI: -1.62 - 3.32, $P = 0.05$; X^2 for heterogeneity, $P = 0.005$)	Pooled mean net change in TC for those treated with a legume diet compared to control was -11.8 mg/dL (95% CI: -16.1 to -7.5); mean net change in LDL-C was -8.0 mg/dL (95% CI: -11.4 to -4.6). Pooled mean net change in TG was -18.94 mg/dL (95% CI: -38.04 - 0.17, $P = 0.05$; X^2 for heterogeneity, $P < 0.001$)

CI: confidence interval; HDL-C: high-density lipoprotein-cholesterol; LDL-C: low-density-cholesterol; RCT: randomized controlled trial; TC: total cholesterol; TG: triglyceride.

3.2% higher ($P < 0.007$) with soy versus control [18]. Soy protein intake was also associated with reduction in serum LDL-C and TG. Soy protein consumption with a median of 30 g/day was associated with a significant improvement in lipoprotein risk factors.

Bazzano et al investigated effects of intake of non-soy legume on serum lipids. Ten RCTs were selected which compared a non-soy legume diet to control, had a minimum duration of 3 weeks, and reported blood lipid changes during intervention and control [19]. Although results indicated that a diet rich in legumes other than soy decreases TC and LDL-C, this study did not show a significant association of intake of non-soy legume with HDL-C due to a significant heterogeneity of collected data [19].

Various mechanisms have been suggested by which soy proteins may exert their lipid-lowering effects. The activation of LDL receptors by essential amino acids from soy protein [20], and soy protein-based inhibition of endogenous cholesterol synthesis [21] have been proposed. Further, water-soluble dietary fiber and other components such as isoflavones may also reduce serum lipid levels [22].

Although the hypocholesterolemic effect of soy is well documented, the underlying mechanisms for soy-mediated increase of HDL remain largely unknown. Soy contains additional components, such as isoflavones, lecithins, saponins and dietary fiber that may improve cardiovascular risk factors by independent mechanisms such as hypoglycemic effect, anti-inflammatory effect and anti-obesity effect [23]. Such additional components in soy may be associated with elevation of HDL-C, which support no effects of non-soy legume on HDL-C.

Conclusions

Intake of soy and non-soy legume was significantly associated with reduction of TC and LDL-C. Intake of soy was significantly associated with elevation of HDL-C; however, non-soy consumption was not associated with a significant increase of HDL.

Conflict of Interest

The authors declare that they have no competing interests.

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