Review

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Effects of Soy Protein and Isoflavones Intake on HDL Metabolism in Asian Populations

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Abstract

High-density lipoprotein (HDL) has been shown to have a variety of functions that contribute to anti-atherogenesis. Therefore, low HDL-cholesterol (HDL-C) level is significantly associated with the development of coronary artery diseases (CADs). Soy and isoflavones have been proposed to reduce the risk of CAD. However, the underlying mechanisms for soy and isoflavone-induced reduction of coronary risks remain largely unknown. To understand effects of lifestyle on lipids metabolism, the existence of interracial differences should be considered. Here we reviewed published articles about effects of soy and isoflavone intake on HDL metabolism. We regarded systematic review and meta-analysis and also clinical studies which were performed in Asian populations as important articles in this review. Evidences obtained from clinical trials performed in Asian populations showed that effects of soy protein and isoflavones on HDL-C were limited, which may be due to limited studied population such as postmenopausal women. Meta-analyses indicated that intake of soy protein and isoflavones is beneficially associated with HDL metabolism.

Keywords: Atherosclerosis; High-density lipoprotein; Isoflavones; Meta-analysis; 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 and isoflavones have been proposed to reduce the risk of CAD. A previous Japanese case-control study suggested that tofu (soybean curd) consumption may be protective against the risk of acute myocardial infarction in women [6]. The Japan Public Health Center-based study also revealed that high isoflavone intake was associated with reduced risk of cerebral infarction and myocardial infarction in Japanese women [7]. However, the underlying mechanisms for soy and isoflavone-induced reduction of risk of atherosclerotic diseases remain largely unknown. To understand effects of lifestyle including dietary factors on lipids metabolism, the existence of interracial differences should be considered.

Here we reviewed published articles about effect of soy and isoflavone intake on HDL metabolism. We regarded systematic review and meta-analysis and also clinical studies which were performed in Asian populations as important articles in this review.

Meta-Analyses to Evaluate Effects of Soy Protein and Isoflavones on HDL Metabolism

Meta-analyses to study effects of soy protein and isoflavones on HDL-C were shown in Table 1. Taku et al conducted a meta-analysis to evaluate effects of soy isoflavones on lipid profiles [8]. The effects of soy protein that contains enriched and depleted isoflavones were also examined. Eleven studies were selected for the meta-analysis. Soy isoflavones showed no significant changes in HDL-C. Soy protein with enriched isoflavones significantly increased HDL-C by 3.0%.

Reynolds et al performed a meta-analysis to examine the effect of soy protein supplementation on serum lipids in adults, by searching MEDLINE (1966 to February 2005) [9]. A total of 41 randomized controlled trials (RCTs) in which isolated soy protein supplementation was the only intervention and the net changes in serum lipids during intervention were reported. Soy protein supplementation was associated

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Table 1. Meta-Analyses to Evaluate Effects of Soy Protein and Isoflavones on High-Density Lipoprotein Cholesterol (HDL-C)

Authors	Aim of study	Subjects studied	Results/conclusions
Taku et al [8]	The meta-analysis to evaluate the precise effects of soy isoflavones on lipid profiles	PubMed was searched for randomized controlled trials published from 1990 to 2006 that described the effects of soy protein intake in humans. Eleven studies were selected for the meta-analysis.	Soy isoflavones did not change HDL-C, and soy protein with enriched isoflavones significantly increased HDL-C by 3.0%.
Reynolds et al [9]	The meta-analysis to examine the effect of soy protein supplementation on serum lipid levels in adults	A total of 41 randomized controlled trials in which isolated soy protein supplementation was the only intervention and the net changes in serum lipids during intervention were reported.	Soy protein supplementation was associated with a significant increase in HDL-C (0.77 mg/dL, 95% CI: 0.20 - 1.34).
Zhan et al [10]	To identify and quantify the effects of soy protein containing isoflavones on lipid profiles	Twenty-three eligible randomized controlled trials published from 1995 to 2002 were identified from the PubMed database.	Soy protein with isoflavones intact was associated with significant increases in serum HDL-C (3.03%).
Weggemans et al [11]	To study specifically the effect of soy-associated isoflavones on cholesterol concentrations in well-controlled trials substituting soy protein with dairy or animal protein	Studies comprised 959 subjects (336 men and 623 women), average age ranged from 41 to 67 years old and baseline cholesterol concentration ranged from 5.42 to 6.60 mmol/L.	Feeding daily 36 g soy protein with 52 mg soy-associated isoflavones on average increased HDL-C by 0.03 ± 0.01 mmol/L.

with a significant increase in HDL-C (0.77 mg/dL, 95% CI: 0.20 - 1.34), and the meta-regression analyses showed a dose-response relation between intake of soy protein and isoflavone supplementation and net changes in serum lipids.

Zhan et al conducted a meta-analysis to identify and quantify the effects of soy protein containing isoflavones on serum lipids [10]. Twenty-three eligible RCTs published from 1995 to 2002 were identified from the PubMed database. Soy protein with isoflavones intact was associated with significant increases in serum HDL-C by 0.04 mmol/L (3.03%). Initial total cholesterol concentrations had a powerful effect on changes in HDL-C. Studies with intakes > 80 mg showed better effects on serum lipids. Improvements in HDL-C were only observed in studies of > 12 weeks duration.

Weggemans et al performed a meta-analysis to study specifically the effect of soy-associated isoflavones on cholesterol concentrations in well-controlled trials substituting soy protein with dairy or animal protein by MEDLINE searches (1995 - 2002) [11]. Studies comprised 959 subjects (336 men and 623 women), average age ranged from 41 to 67 years and baseline cholesterol concentration ranged from 5.42 to 6.60 mmol/L. Feeding daily 36 g soy protein with 52 mg soy-associated isoflavones on average increased HDL-C by 0.03 ± 0.01 mmol/L. There was no dose-response relation between soy-associated isoflavones and HDL-C (correlation coefficient: -0.07; P = 0.76).

Evidences obtained from meta-analyses showed that intake of soy protein and isoflavones is beneficially associated with HDL metabolism.

Clinical Trials to Study Effects of Soy Protein and Isoflavones on HDL Metabolism in Asian Populations

Clinical trials to study effects of soy protein and isoflavones on HDL-C in Asian populations were shown in Table 2. Liu et al studied the effects of moderate intake of soy protein (15 g) with isoflavones or isoflavones alone on serum lipids in

Table 2. Randomized, Placebo-Controlled Trials to Evaluate Effects of Soy Protein and Isoflavones on High-Density Lipoprotein Cholesterol (HDL-C), Performed in Asian Populations

Authors	Nationality of subjects	Subjects studied	Study design	Results/conclusions
Liu et al [12]	Hong Kong	180 postmenopausal Chinese women with prediabetes or early untreated diabetes, aged 46-70 years and, on average, 6.0 years since menopause	Participants were randomly assigned to one of the three arms to receive 15 g soy protein and 100 mg isoflavone, or 15 g milk protein and 100 mg isoflavone or 15 g milk protein on a daily basis for 6 months.	No significant difference was observed in serum HDL-C between the three groups at both 3 and 6 months.
Ye et al [13]	China	Ninety early postmenopausal Chinese women, aged 45 to 60 years	Subjects were randomly assigned to three treatment groups (30 each) receiving daily doses of 0 (placebo), 84, and 126 mg of soy germ isoflavones.	No significant differences were observed in serum lipids.
Ho et al [14]	Hong Kong	203 postmenopausal Chinese women aged 48 to 62 years	Subjects were randomly assigned to receive daily doses of 500 mg calcium, and 0 mg isoflavones (placebo, n = 67), 40 mg isoflavones (n = 68) and 80 mg isoflavones (n = 68).	Little effect of soy isoflavones on changes in serum lipids was observed among the treatment groups.
Wu et al [15]	Japan	A total of 136 postmenopausal women at < 5 years after the onset of menopause	Subjects were randomly assigned to four groups: placebo, walking (45 min/day, 3 days/week) with placebo, isoflavone intake (75 mg of isoflavone/day) and combination of isoflavone plus walking.	Serum HDL-C significantly increased by 12 months after the walking and the combined intervention.
Wu et al [15]	Japan	128 postmenopausal women	Subjects were randomly assigned to 4 groups: placebo; placebo combined with walking (3 times/week); isoflavone intake (75 mg of isoflavones/day); and isoflavone combined with walking.	Serum HDL-C significantly increased (6.1%, P = 0.03) from the baseline in the combined intervention group.

180 Chinese postmenopausal, prediabetic women, aged 46-70 years and, on average, 6.0 years since menopause [12]. Participants were randomly assigned to one of the three arms to receive 15 g soy protein and 100 mg isoflavone, or 15 g milk protein and 100 mg isoflavone or 15 g milk protein on a daily basis for 6 months. The results showed that no significant difference was observed in serum HDL-C between the three groups at both 3 and 6 months.

Ye et al examined the effect of soy germ isoflavones on serum lipids [13]. Ninety early postmenopausal Chinese women, aged 45 to 60 years, were randomly assigned to three treatment groups (30 each) receiving daily doses of 0 (placebo), 84 and 126 mg of soy germ isoflavones. No significant differences were observed in serum lipids.

Ho et al examined the effects of isolated soy germ isoflavones on the changes in serum lipids [14]. RCT was conducted in 203 postmenopausal Chinese women aged 48 to 62 years. They were randomly assigned to receive daily doses of 500 mg calcium, and 0 mg isoflavones (placebo, n = 67), 40 mg isoflavones (n = 68) and 80 mg isoflavones (n = 68). They observed little effect of soy isoflavones on changes in serum lipids among the treatment groups.

Wu et al studied the effects of isoflavone intake, walking exercise and their interaction on lipid metabolism over 1 year in postmenopausal Japanese women [15]. A total of 136 postmenopausal women at < 5 years after the onset of menopause were randomly assigned to four groups: placebo, walking (45 min/day, 3 days/week) with placebo, isoflavone intake (75 mg of isoflavone conjugates/day), and combination of isoflavone plus walking. Serum HDL-C significantly increased by 12 months after the walking and the combined intervention.

Wu et al also performed one more study to evaluate effects of isoflavone intake and walking and their interaction on serum lipid metabolism in postmenopausal women over 24 weeks [16]. One hundred twenty-eight subjects were randomly assigned to four groups: placebo; placebo combined with walking (3 times/week); isoflavone intake (75 mg of isoflavones conjugates/day); and isoflavone combined with walking. Serum HDL-C significantly increased (6.1%, P = 0.03) from the baseline in the combined intervention group.

Three RCTs showed that soy and isoflavone intake is not associated with increases in HDL-C in postmenopausal women. Two RCTs showed significant increases in HDL-C due to soy and isoflavone intake in postmenopausal women; however, these increases were only observed by combination with walking.

Conclusions

Evidences obtained from RCTs performed in Asian populations showed that effects of soy protein and isoflavones on HDL-C were limited, which is may be due to limited studied population such as postmenopausal women. Meta-analyses indicated that intake of soy protein and isoflavones is beneficially associated with HDL metabolism.

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Conflict of Interests

The authors declare that they have no competing interests.

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