Effects of Soy on Metabolic Biomarkers of Cardiovascular Disease in Elderly Women with the Metabolic Syndrome

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Abstract

Objective: To ascertain the effects of soy [in the forms of Textured Soy Protein (TSP) and soy–nut] on lipid profiles, apolipoproteins, inflammatory and prothrombotic markers and blood pressure in elderly women with the metabolic syndrome.

Materials and methods: The study is a 12–week parallel randomized controlled trial that was conducted in rural health centres of Babol, Iran. The participants were 75 women 60–70 years old with the metabolic syndrome who were randomized to one of the three groups of soy–nut (35g/d), TSP (35g/d) and control. Blood pressure and blood biochemical markers were measured at baseline and at the end of the study including, triglyceride, cholesterol, HDL–C, LDL–C, VLDL–C, $ApoB_{100}$, ApoAI, CRP and fibrinogen.

Results: The soy–nut improved significantly LDL–C, VLDL–C and Apo B_{100} ($P<0.05$) while fewer improvements but significant were observed in these variables in the TSP group only when compared with the mean changes from the baseline ($P<0.001$). Similar result was found for Apo AI in the treatment groups ($P<0.01$). Serum total cholesterol decreased significantly in the treatment groups compared with control group ($P<0.005$). The differences from control for triglyceride, HDL–C, fibrinogen, CRP and blood pressure were not significant.

Conclusion: Both forms of soy while improved lipids profiles the soy–nut contribution was more to this improvement than the TSP. Therefore, moderate daily intake of soy may be a safe, cheap and practical method to improve cardiovascular disease risk and also reduce the need for medical treatment.

Keywords: Aging, dyslipidemia, Inflammatory factor, Metabolic syndrome, Soy foods

Introduction

The Metabolic Syndrome (MS) has emerged as a cluster of risk factors for atherosclerotic diseases. Dyslipidemia with proinflammatory and procoagulant status associated with MS ultimately leads to cardiovascular complications in these patients (1, 2). It is suggested that proinflammatory status play an essential role in pathophysiology of MS through the enhanced adipose tissue derived cytokine expression and

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Table 1: Nutrient Composition of Soy Nut and Textured Soy Protein Used In the Study*

Nutrients per 100 g	Textured Soy protein	Soy–nut
Protein (g)	52	39.5
Fat (g)	1.3	25
Total carbohydrate (g)	32.5	33
Fiber (g)	34	30
Aglycone isoflavones (mg)	275	335
Diadzein (mg)	110	136
Genistein (mg)	139.5	172
Glycitein (mg)	25.5	27

* Amounts are per 100 g.

therefore an insulin resistance (3). Fibrinogen and CRP as acute–phase proteins increase in response to a high–cytokine state. Thus, they may be metabolically interconnected and is used as a screening tool for individual high risk for cardiovascular disease (CVD) (4). Thereby reducing the levels of these proteins can be a practical target for new therapies for individuals with MS. Dyslipidemia and inflammatory markers increase with age and especially in women due to multiple age–related physiological mechanisms and endocrine changes from menopause (1,5).

Hence, older women with MS are at high risk of heart disease. Nutrition has a major role in the MS (6) (8). Several studies have been conducted on the effect of diet on lipid profile and inflammatory markers especially the effect of soy intake; however, most of them have been done on healthy people or hypercholesterolemic and diabetic patients (9–14). On the other hand the results of these studies are contradictory (15). Soy is a plant–derived estrogen that through its anti–inflammatory and antilipemic properties may protect against CVD (10).

To our knowledge no comprehensive reports are available regarding the effects of soy–nut as natural state of soybean against textured soy protein (TSP), as a processed soy product on metabolic biomarkers of the MS only in women ≥ 60 years. This research evaluates the effects of two types of soy on lipid profiles, apolipoproteins, CRP, fibrinogen and blood pressure among older women with the MS.

Materials and Methods

Participants

The study, was approved by the "Ethics Committee" of University Putra Malaysia and Babol University of Medical Sciences, Iran. A total of 200 women of 60–70 years old were screened to include in the study. The study was conducted in rural health centers of Babol, Iran in 2009. The MS was determined according to Adult Treatment Panel (ATP III guidelines: 1) waist circumference >80 cm; 2) serum HDL–C < 50 mg/dL; 3) triglyceride ≥ 150 mg/dL; 4) fasting blood glucose ≥100 mg/dL; and 5) systolic blood pressure ≥ 130 mmHg and diastolic ≥ 85 mmHg. To be enrolled in the study, subjects had to have ≥ 3 of the above-mentioned criteria without the need to drug for treatment of diabetes, hypertension, and hyperlipidemia. Exclusion criteria were: currently or previously using estrogen therapy, soy products or supplements, treatment with aspirin, antibiotic, history of CVD, hyper and hypothyroidism, kidney, liver, infectious diseases, breast cancer or any cancer, vegetarian, smoking and allergic reaction to soy consumption. Finally, a total of 75 women of 60–70 years old who met the inclusion criteria were included in the study. All participants provided informed written consent.

Study procedures

This study was a 12–week parallel randomized controlled trial. The subjects were randomized into three groups. Group A received 35 g soy–nut (n=25) and group B 35 g TSP (n=25) daily for three months. Group C received nothing as a control group (n=25). Soy–nut and TSP were packed in 490 grams small bags for 2 weeks consumption and provided a soy dose of 35 grams daily. The nutrient composition soy is shown in Table 1. The people in group B were trained on how they could prepare their meal with TSP. Soy–nut and TSP are produced and packed by Max Soy Company in Tehran, Iran.

The participants were asked not to change their habitual diet and physical activity levels for the duration of the study. To assure to not change in diet and activity, dietary intake and physical activity level, all were measured at baseline during each month intervention. Each participant brought her 3–d dietary intake and physical activity records (recorded as MET–min-

Table 2: The Macronutrient and Micronutrient Intake (Mean±SE) of the Participants in the Treatment and the Control Groups

	Treatment Groups		Control (n=25)	*P*–Value†
	Soy–nut (n=25)	TSP (n=25)		
Total Calorie (kcal)	1943±50.4	1939±53.3	1959±54.6	0.52
CHO (g) Percentage	267.2±30.1 55±3.2	275.3±31.1 56.8±4.2	277.2±30.1 56.6±3.1	0.35
Protein (g) Percentage	74.9±8.2 15.4±3	81.4±9.2 16.8±3.3	79.8±8.5 16.3±3.1	0.24
Total Fat (g) Percentage	63.9±9.1 29.6±5.6	56.8±8.5 26.4±5.3	58.9±9.7 27.1±5.9	<0.05
SFA (g) Percentage	11.9±3.8 5.5±1.7	11.6±2.9 5.4±1.3	16.5±4.7 7.6±2.2	<0.001
MUFA (g) Percentage	20±5.2 9.25±1.5	20.5±5.4 9.5±1.6	19.6±5.1 9±1.5	0.51
PUFA (g) Percentage	31.9±7.4 14.8±2.8	24.8±6.5 11.5±2.4	22.8±6.1 10.5±2.2	<0.001
Fiber (g)	39.3±8.2	40.8±9.2	25.3±5.1	<0.001
Phosphorus (mg)	803±20	550±21	400±19	<0.001
Potassium (mg)	3684±176	2420±179	2297±185	<0.001
Calcium (mg)	1110±92	1080±88	770±76	<0.001
Folic Acid (mcg)	170±30	168.81±27	170.80±29	0.82
Magnesium (mg)	450±5	320±5	300±5	<0.001
Zinc (mg)	11.81±5.6	10.21±3.7	10.94±4.7	0.14
Iron (mg)	20.74±6.6	19.76±6.9	20.35±78	0.27
Vit A(RE)	8282±65	8380±60	8250±66	0.38
Vit E (mg)	8.41±1.5	8.22±1.5	8.62±1.4	0.22
Vit C (mg)	70.9±12	69.1±12	72.1±12	0.87
Vit B_1 (mg)	1.1±0.49	1.2±0.67	1.0±0.59	0.52
Vit B_2 (mg)	1.7±0.47	1.4±0.5	1.9±0.4	0.29
Vit B_6 (mg)	0.76±0.1	0.71±0.09	0.92±0.1	0.27
VitB_{12} (mcg)	2.1±0.6	1.9±0.7	2.1±0.6	0.26

TSP, textured soy protein; SE, standard Error; CHO, carbohydrate; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; †*P*–Values is related to the differences in the three groups under study (GLM Repeated Measures). The two tailed P<0.05.

utes/week using IPAQ) every month and handed in to the researcher. These questionnaires were analyzed in controlling the participant's compliance and making sure there were no changes in diet and physical activity level throughout treatment period.

The participants were visited every two weeks and were called on weekly for monitoring compliance, any complain about soy or any changes in their health status. In every two–week meeting, empty packages were taken back and new packages were given to be used for the next two weeks. Monthly visits were done to pick up the completed questionnaires of physical activity and 3–d dietary intake record of the participants of all three groups and also to measure their

blood pressure. The metabolic biomarkers were measured on all three groups before and after three months intervention.

Measurements

After 10–12 hours overnight fasting, 10 ml of venous blood was drawn; 1.8 ml the blood samples were collected in citrated tubes for measuring fibrinogen. The rest the blood samples were collected into test tubes. Serum was separated by centrifugation within 15 minutes of collection. The aliquots were frozen and stored at −80°C for subsequent analyses.

The total cholesterol (TC) and triglyceride (TG) levels were measured using Elitech kit from France and LDL–C, HDL–C and VLDL–C by Pars Azmoon kit from Iran.

All lipid profiles were assayed on Mindray–BS300, chemistry Autoanalyzer (Mindray–BS300, Nanshan, Shenzhen, China). Apo AI and Apo B_{100} were measured by ELISA method (Diagnostic Mabteck AB, Sweden). Fibrinogen was analyzed one hour (at the latest) after sampling using MAHSA–YARAN kit, Iran, through quantitative determination of plasma fibrinogen by a Clauss method (clotting method) using the guidelines from MAHSA–YARAN Company. The quantity of CRP in serum was determined by a human microplate immunoenzymetric assay (AccuBind ELISA Kit, Monobind Inc., Costa Mesa, USA). Blood pressure of the participants was assessed twice at the right arm after 10 minutes sitting by using a calibrated mercury sphygmomanometer. The average of two seated systolic and diastolic blood pressure measurements were used for data analysis.

Statistical analysis

One–way ANOVA test was conducted to compare the baseline and end values of the variables in the three groups. Changes from the baseline within each group were evaluated using the paired *t* test and between–group changes were tested by the ANOVA. Also, the mean differences were determined by calculating the differences in change value for each variable in pair–wise group comparisons using the ANOVA test. The Generalized Linear Model (GLM) repeated measures analysis, two factor mixed design was applied to detect the changes in mean of physical activity level and dietary intake of the participants during the 12–week intervention. Blood pressure was analyzed by Kruskal–Wallis test. The two–tailed *P*.value less than 0.05 was considered significant. Statistical analysis was performed using SPSS windows version 17.

Results

All participants completed the entire study. Table 2, shows the mean intake of nutrients by the participants in all three groups during the treatment period. The mean±SE total physical activity level (MET–minutes/week) of the participants remained the same during the study (in the soy–nut group: 2824.5±189.19; in the TSP group: 2769.2±233.16; and in the control group: 2850± 175.39) .

Metabolic biomarkers, including serum lipid profiles, apolipoproteines, CRP, plasma fibrinogen and also blood pressure are shown in Table 3. No significant difference in the baseline values of these variables was observed. After intervention, mean of TC, LDL–C, VLDL–C and Apo B_{100} in the soy–nut group was significantly lower than in the control group ($P<0.05$), while TSP intake only leads to the lower level of TC compared to the control group ($P<0.05$). The mean difference from the control group demonstrated significantly reduction after soy–nut and TSP intake for TC (20.54±5.9, $P<0.003$; 15.6±6, $P<0.03$), LDL–C (22.27±4.2, $P<0.001$; 19.32±4.2, $P<0.001$), VLDL–C (6.7±1.46, $P<0.001$; 4.65±1.47, $P<0.007$), Apo B (0.37 ±0.05, $P<0.001$; 0.35±0.05, $P<0.001$) and a significant increase in Apo AI (–0.21±0.08, $P<0.02$; –0.2±0.08, $P<0.03$). The mean change for TG and HDL–C was not significant although they showed a more reducetion in the treatment groups (Table 4). Comparison of the two treatment groups together showed decrease in TC, TG, LDL–C, and VLDL–C in the nut group was higher than the TSP group, while mean changes in serum levels of HDL–C, Apo AI and Apo B_{100} between the two groups were almost similar. However significant difference between these two groups for lipid profile was not seen. There were no significant differences in the end values or mean change of CRP, fibrinogen and blood pressure in the groups.

Discussion

The results of the present study showed that daily consumption of 35 g of soy, both soy–nut and TSP for 12 weeks has beneficial effects on lipid profiles and apolipoproteines, while has no effect on CRP, fibrinogen and blood pressure in elderly women with the MS. Moreover, the effects of soy–nut were found more appropriate in comparison with TSP.

In this study, consuming both soy–nut and TSP resulted in decreasing in serum TC, LDL–C, VLDL–C, Apo B_{100}, and increasing Apo AI. Also, the percentage changes for TG and HDL–C were –5.8 %, +4.7 % in the nut and –5.5 %, +4.03% in the TSP groups

Table 3: Mean± SD of Blood Pressure, Lipid Profiles, CRP, and Fibrinogen in the Treatment and Control Groups before and after Intervention

Lipid profiles	Baseline			After Intervention			
	Soy–nut	TSP	Control	*P*–Value	Soy–nut	TSP	Control	*P*–Value
SBP (mmHg)	127.29±4.41	127.60 ±4.48	127.38±4.64	0.97	123.12±6.56	124.34±7.43	126.42±4.78	0.22
DBP (mmHg)	79.37±6.47	80.65±4.34	81.42±6.15	0.48	75.83±8.68	78.69±5.26	80±2.73	0.07
TC (mg/dl)	229.95±25.17	229.47±28.03	233.19 ±23.86	0.86	200.75±23.76†	205.17±26.6†	224.52 ±23.8	<0.001
TG (mg/dl)	212.12±40.3	211.95±42.5	212.6±48.8	0.9	199.8±42.4	200.3±43.5	208.5±49.4	0.7
HDL–C (mg/dl)	44.2±6.76	43.08±4.71	44.23±7.25	0.78	46.29±5.7	44.82±4.4	43.7 ±7.8	0.3
LDL–C (mg/dl)	154±28.4	154.69±28.8	152.28±25	0.9	131±25.27†	134.56±27.1	151.47±29.8	<0.05
VLDL–C (mg/dl)	41.69±7.69	42.39 ±8.5	42.38 ±10	0.95	34.55± 8.9†	37.36±9.7	42±9.9	<0.05
Apo AI (g/l)	1.8±1.02	1.78±1.1	1.6±1	0.77	2±1	1.96±1	1.58±0.9	0.3
Apo B100 (g/l)	1.48±0.48	1.5±0.5	1. 52±0.8	0.96	1.16±0.4†	1.21±0.5	1.59±0.7	<0.05
CRP (µg/ml)	3.16±1.8	3.13±2.16	3.01±2.28	0.97	2.9±1.9	2.96±1.9	3±1.54	0.98
Fibrinogen (mg/dl)	316.7±33.79	316.56±42.61	314.19±42.95	0.97	297.87±29.75	302±30.57	306.42±30.2	0.63

TSP: textured soy protein; SD: standard deviation; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL–C: high density lipoprotein; LDL–C: low density lipoprotein; VLDL–C: very low density lipoprotein; Apo AI: Apolipoprotein A1, Apo B100: Apolipoprotein B100; CRP, C – reactive protein.
† Significant difference between treatment groups with control (Post hoc tests). The two tailed P< 0.05.

Table 4: Mean changes and mean difference ±SE for Blood Pressure, Lipid Profiles, CRP and Fibrinogen after intervention

Lipid profiles	Mean Change ± SE			*P*–Value	Mean Difference ± SE		
	Soy–nut	TSP	Control		Control and TSP (*P*–Value)	Control and Soy–nut (*P*–Value)	TSP and Soy–nut (*P*–Value)
SBP (mmHg)	–4.2±1.3	–3.3±1.5	–0.95±1.2	0.24	2.3±1.96 (0.47)	3.21±1.94 (0.23)	0.9±1.89 (0.88)
DBP (mmHg)	–3.5±1.81	–1.9±1.36	–1.4±1.15	0.58	0.52±2.15 (0.96)	2.1±2.13 (0.58)	1.58±2.08 (0.72)
TC (mg/dl)	–29.2±3.56	–24.3±3.5	–8.7±5.4	<0.0·1	15.6±6.03 (<0.05)	20.5±5.9 (<0.001)	4.9±5.8 (0.67)
TG (mg/dl)	–12.2±1.8	–11.6±1.9	– 4.1±1.12	0.14	7.6±4.53 (0.22)	8.2±4.49 (0.17)	0.59±4.38 (0.99)
HDL–C (mg/dl)	2.1±0.5	1.7±0.6	– 0.57±1.4	0.1	–2.3±1.32 (0.19)	–2.6±1.31 (0.11)	–0.34±1.28 (0.96)
LDL–C (mg/dl)	–23.1±2	–20.1±3	–0.80±3.8	<0.001	19.3±4.28 (<0.001)	22.3±4.23 (<0.001)	2.9±4.13 (0.75)
VLDL–C (mg/dl)	–7.1±1.1	–5±0.67	– 0.37±1.2	<0.001	4.7±1.47 (<0.001)	6.7±1.46 (<0.001)	2.11±1.42 (0.3)
Apo AI (g/l)	0.19±0.03	0.18±0.03	–0.02±0.01	<0.01	– 0.2±0.08 (<0.05)	–0.21±0.08 (<0.05)	– 0.01± 0.04 (0.8)
Apo B100 (g/l)	–0.31±0.04	–0.28±0.01	0.06 ±0.05	<0.001	0.35±0.05 (<0.001)	0.37±0.05 (<0.001)	0.02±0.05 (0.9)
CRP (µg/ml)	–0.25±0.16	–0.16±0.17	–0.04±0.32	0. 8	0.12±0.32 (0.92)	0.21±0.32 (0.78)	0.09±0.31 (0.95)
Fibrinogen (mg/dl)	–18.8±8.98	–14.5±9.53	–7.8±6.2	0.65	6.7±12.23 (0.84)	11.07± 12.1 (0.63)	4.31±11.8 (0.93)

TSP=Textured Soy Protein; SE, standard error; TC, total cholesterol; TG, triglyceride; HDL–C, high density lipoprotein; LDL–C, low density lipoprotein; VLDL–C, very low density lipoprotein; Apo AI, apolipoprotein AI, Apo B100, apolipoprotein B100; CRP, C – reactive protein. The two tailed P <0.05.

respectively, though this reduction was not statistically significant. The results of this intervention are consistent with the results of three comprehensive reviews on soy consumption and measures of cardiovascular health (16–18). All three reports concluded that there was a significant effect of soy–nut (16) and TSP[17–18] containing isoflavones when consumed at levels similar to this research on LDL–C (11%–15.3%), TC (7.5%–17.2%) and Apo B_{100} (8%–14.6%) but not on HDL–C or TG concentrations (17–20). The clinical significance of soy intake on HDL–C concentration has remained controversial. However, among the previous reports, even those with a high isoflavone intake, only a few studies observed had significant changes in the HDL–C level (11).

The different results in different studies can be addressed by Zhan and Ho's study. They, in a meta–analysis on 23 clinical trials, reported that higher initial TC concentrations and intakes >80 mg isoflavone have better effects on the lipid profile. Also, the strongest lowering effects of soy protein on TC and LDL–C occurred within the short initial period of intervenetion, whereas improvement in HDL–C was only observed in lengthy studies i.e. more than12 weeks (20). Another reason may be the difference in 7S globulin concentration among soy varieties in the different studies (21–22). The results of this study, consistent with two recent studies showed that serum level of Apo AI increased significantly in the treatment groups (17–19) while the significant increase in Apo AI did not correspond with the results of HDL–C because no significant increase in the level of HDL–C was observed. The difference in change in Apo AI (11%) versus the change in HDL–C (4.7%) is unclear because there is one Apo A molecule in the HDL particle.

One explanation could be that the particle size of HDL in hyperlipidemic subjects shifted towards smaller sizes, which in turn, indicates HDL–C maturation might be abnormal in hyperlipidemic subjects. Another argument is that the HDL–C levels, in contrast to the Apo AI levels, are calculated but not measured which may have led to an underestimation in HDL–C change and to some extent explains the difference. Hermansen *et al.* also found the apparent differences in change of Apo B (30%) versus the change in LDL –C (10%) (23). However, though improvements in HDL–C and TG measurements were not significant, their importance is similar to reductions in TG and HDL–C levels observed in other studies (20–24) and may have clinical relevance especially since TG and HDL-C level are stronger predictors of cardiovascular risk in women than in men.

The proposed mechanisms for a hypocholesterolemic effect of soy are:

1) The higher arginine to lysine and methionine amino acid profile of soy protein (17)
2) Up–regulate LDL receptors by 7S globulin protein exist in soy (21–22)
3) Soy fiber content (25)
4) Isoflavones content (26)
5) The trace components such as plant sterols, phytates, folates and oxalates that could be altered by the processing method of the soy products (17).

About the two types of soy products used in this study, Matthan and et al (2007) agreed on soy protein rather than on soy isoflavones as the responsible nutrient. Interestingly, they showed processing of the soy products appeared to have had little effect on their influence on lipid (17).

This finding confirms the results of this study that TSP has a positive effect in improvement of lipid profile like soy–nut, though this effect was less than soy–nut. By comparing the composition of food in the two groups (Table 2), this difference might be attributed to higher values of PUFA, isoflavone and micronutrients such as magnesium, calcium, potassium and phosphorus in the soy–nut than TSP.

The results of this study showed that consumption of soy–nut and TSP led to 8.2% and 5.43% reduction in CRP levels, though this difference was not significant. Researchers showed that genistein has anti–inflammatory effect in vitro and in vivo (13). Although a recent meta–analysis to assess the 14 RCT reported that neither soy foods nor soy isoflavone has effect on biomarkers of inflammation (27). Results of recent study are consistent with many published studies evaluating the effects of acute consumption of soy on CRP concentration (17,28–32) while some others showed the positive effect of soy on CRP in long–term experiments (33–34). Considering all the factors, a possible explanation for the differences in results is that the dose used in this study (35 g/d) was insufficient and higher amounts might have produced better results for CRP. However, high doses may be connected to some other health risks (35). Also, it is possible that the effects mediated by the isoflavone are too modest to be detected over the 3 months study period, while most effective trials about the use of soy and CRP level have been done something about a year (33–34). The global level CRP of the participants in this study at the baseline was 3.1 g/ml, whereas it is possible

that soy protein has a positive effect only in persons with more elevated CRP.

The findings suggest hyperfibrinogenemia (>350 mg/dl) as a component of the MS may explain the increased cardiovascular risk (36). There are reports that the formation of thrombin and platelet activity is inhibited by genistin in vitro (37). In this study, although procoagulant fibrinogen level did not reach statistical significance, but it decreased 5.9% by consuming 117 mg isoflavone *vs* 4.6% of 96 mg isoflavone. Dent *et al*. (2001) showed no change in fibrinogen with consumption of 40 g/d soy protein in six months (38). Also study of Hermansen *et al.* (2001) on consuming 50 g/d soy protein with 165 mg/day isoflavone in diabetic patients reported a non–significant decrease in fibrinogen value (23). These results are consistent with those obtained in current study.

In the present study, TSP and soy–nut did not create a significant reduction in blood pressure. Some studies have reported beneficial effects of soybean on blood pressure (16,36). It is not quite clear whether this beneficial effect is related to the isoflavone content, protein of soy or higher concentration of proteins rich in specific amino acids (39). However, several studies did not report significant effects of soy protein intake on blood pressure containing isoflavone (11,17,23,28). This difference can partly be related to the characteristics of the participants because the studies about the effect of soy on blood pressure were done often in healthy or hypertensive people in different age and sex groups while the current study was conducted exclusively on elderly women with the MS. Physiologic changes during the aging process with the MS can make the answer to the treatment more complicated.

We had not taken into consideration equal production capacity of individual in response to soy intake, so more researches are needed to investigate the relationship between equal production and response to soy intake.

Conclusions

The results of this study showed that soy inclusion as part of the daily diet has a beneficial effect on atherogenic lipids in older women with the MS. Meanwhile the effect of soy–nut was more significant than TSP. This study did not show any significant improvement in blood pressure, CRP and fibrinogen levels. Although the soy effect on lipid profiles was known better, but anti–inflammatory and anticoagulant mechanisms of soy in human are not very well known yet and more research is needed to further this study in effect.

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References

1. Kaaja RJ. Metabolic syndrome and the menopause. *Menopause Int* 2008; 14: 21–5.
2. Handelsmn Y. Metabolic Syndrome Pathophysiology and Clinical Presentation. *Toxicol Pathol* 2009; 37: 18–20.
3. Odrowaz–Sypniewska G. Markers of pro–inflammatory and pro–thrombotic state in the diagnosis of metabolic syndrome. *Adv Med Sci* 2007; 52: 246–50.
4. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome: a new world–wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med.* 2006; 23: 469–80.
5. Eshtiaghi R, Esteghamati A, Nakhjavani M. Menopause is an independent predictor of metabolic syndrome in Iranian women. *Maturitas* 2010; 65: 262–6.
6. Lutsey PL, Steffen LM, Stevens J. Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study. *Circulation* 2008; 117:754–61.
7. Feldeisen SE, Tucker KL. Nutritional strategies in the prevention and treatment of metabolic syndrome. *Appl physiol Nutr Metab* 2007; 32: 46–60.
8. Djoussé L, Padilla H, Nelson TL, Gaziano JM, Mukamal KJ. Diet and metabolic syndrome. *Endocr Metab Immune Disord Drug Targets* 2010; 10: 124–37.
9. McVeigh BL, Dillingham. BL, Lampe JW, Duncan AM Effect of soy protein varying in isoflavone content on serum lipids in healthy young men. *Am J Clin Nutr* 2006; 83: 244 –51.

10. Hall WL, Vafeiadou K, Hallund J, Bugel S, Reimann M, Koebnick C, Zunft HJ et al. Soy–isoflavone–enriched foods and markers of lipid and glucose metabolism in postmenopausal women: interactions with genotype and equol production. Am J Clin Nutr 2006; 83: 592–600.
11. Sacks FM, Lichtenstein A, Van Horn L, Harris W, Kris–Etherton P, Winston M,et al. Soy protein, isoflavones, and cardiovascular health: an American Heart Association Science Advisory for professionals from the Nutrition Committee. *Circulation*. 2006; 113: 1034–44.
12. Jenkins DJ, Kendall CW, Jackson CJ, Connelly PW, Parker T, Faulkner D et al. Effects of high– and low–isoflavone (phytoestrogen) soy foods on inflammatory biomarkers and proinflammatory cytokines in middle–aged men and women. *Metabolism* 2002; 51: 919–24.
13. Sakai T, Kogiso M. Soy isoflavone and immunity. *J Med Invest.* 2008; 55: 167–73.
14. Hanachi P, Golkho S. Assessment of soy phytoestrogens and exercise on lipid profiles and menopause symptoms in menopausal women. *J Biol Sci* 2008; 8: 789–93.
15. Moutsatsou, P. The spectrum of phytoestrogens in nature: our knowledge is expanding. *Hormones* 2007; 6: 173–93.
16. Welty FK, Lee KS, Lew NS. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. *Arch Intern Med* 2007; 167: 1060–7.
17. Matthan NR, Jalbert SM, Ausman LM, Kuvin JT, Karas RH, Lichtenstein AH.. Effect of soy protein from differently processed products on cardiovascular disease risk factors and vascular endothelial function in hypercholesterolemic subjects. *Am J Clin Nutr* 2007; 85: 960–6.
18. Chen ST, Chen JR, Yang CS, Peng SJ, Ferng SH. Effect of soya protein on serum lipid profile and lipoprotein concentrations in patients undergoing hypercholesterolaemic haemod ialysis. *Br J Nutr* 2006; 95: 366–71.
19. Pipe EA, Gobert CP, Capes SE, Darlington GA, Lampe JW, Duncan AM. Soy protein reduces serum LDL cholesterol and the LDL cholesterol: HDL cholesterol and apolipoprotein B: apolipoprotein A–I ratios in adults with type 2 diabetes. *J Nutr* 2009; 139: 1700–6.
20. Zhan S, Ho SC.. Meta–analysis of the effects of soy protein containing isoflavones on the lipid profile. *Am J Clin Nutr* 2005; 81: 397–408.
21. Duranti M, Lovati MR, Dani V, Barbiroli A, Scarafoni A, Castiglioni S, Ponzone C, et al. The alpha' subunit from soybean 7S globulin lowers plasma lipids and upregulates liver beta–VLDL receptors in rats fed a hypercholesterolemic diet. *J Nutr* 2004; 134: 1334–9.
22. Moriyama T, Kishimoto K, Nagai K, Urade R, Ogawa T, Utsumi S, et al.Soybean beta–conglycinin diet suppresses serum triglyceride levels in normal and genetically obese mice by induction of beta–oxidation, downregulation of fatty acid synthase, and inhibition of triglyceride absorption. *Biosci Biotechnol Biochem* 2004; 68: 352–9.
23. Hermansen K, Søndergaard M, Høie L, Carstensen M, Brock B.. Beneficial Effects of a Soy–Based Dietary Supplement on Lipid Levels and Cardiovascular Risk Markers in Type 2 Diabetic Subjects. *Diabetes Care* 2001; 24: 228–33.
24. Borodin EA, Menshikova IG, Dorovskikh VA, Feoktistova NA, Shtarberg MA, Yamamoto T, et al. Effects of two–month consumption of 30 g a day of soy protein isolate or skimmed curd protein on blood lipid concentration in Russian adults with hyperlipidemia. *J Nutr Sci Vitaminol*. 2009; 55 (6): 492–7.
25. Galisteo M, Duarte J, Zarzuelo A. Effects of dietary fibers on disturbances clustered in the metabolic syndrome. *J Nutr Biochem* 2008; 19: 71–84.
26. Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol–lowering effects of dietary fiber: a meta–analysis. *Am J Clin Nu*tr 1999; 69: 30–42.
27. Beavers KM, Jonnalagadda SS, Messina MJ. Soy consumption, adhesion molecules, and pro–inflammatory cytokines: a brief review of the literature. *Nutr Rev* 2009; 67: 213–21.
28. Jenkins DJ, Kendall CW, Jackson CJ, Connelly PW, Parker T, Faulkner D, et al. Effects of high– and low–isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. *Am J Clin Nutr* 2002; 76: 365–72.
29. Blum A, Lang N, Peleg A, Vigder F, Israeli P, Gumanovsky M, et al. Effects of oral soy protein on markers of inflammation in postmenopausal women with mild hypercholesterolemia. *Am Heart J* 2003; 145: e7.
30. Hanson LN, Engelman HM, Alekel DL, Schalinske KL, Kohut ML, Reddy MB.. Effects of soy isoflavones and phytate on homocysteine, C–reactive protein, and iron status in postmenopausal women. *Am J Clin Nutr* 2006; 84: 774–80.
31. Nikander E, Metsa–Heikkila M, Tiitinen A. Evidence of a lack of effect of a phytoestrogen regimen on the levels of C–reactive protein, E–selectin, and nitrate in

postmenopausal women. *J Clin Endocrino Metab* 2003; 88: 5180–5.
32. Christie DR, Grant J, Darnell BE, Chapman VR, Gastaldelli A, Sites CK. Metabolic effects of soy supplementation in postmenopausal Caucasian and African American women: a randomized, placebo–controlled trial. *Am J Obstet Gynecol* 2010; 203: 153. e1–9.
33. Li Z, Hong K, Saltsman P, DeShields S, Bellman M, Thames G, Liu Y, et al. Long–term efficacy of soy–based meal replacements vs. an individualized diet plan in obese type II DM patients: relative effects on weight loss, metabolic parameters, and C–reactive protein. *Eur J Clinl Nutr* 2005; 59: 411–8.
34. Azadbakht L, Atabak S, Esmaillzadeh A. Soy protein intake, cardiorenal indices, and C–reactive protein in type 2 diabetes with nephropathy: a longitudinal randomized clinical trial. *Diabetes Care* 2008; 31: 648–54.
35. Helferich WG, Andrade JE, Hoagland MS. Phytoestrogens and breast cancer: a complex story. *Inflammopharmacology*. 2008; 16: 219–26.
36. Ma J, Xu A, Jia C, Liu L, Fu Z, Dong J, Guo X, Su J, Bi Z. Associations of fibrinogen with metabolic syndrome in rural Chinese population. *J Atheroscler Thromb* 2010; 17: 486–92.
37. Kondo K, Suzuki Y, Ikeda Y, Umemura K. Genistein, an isoflavone included in soy, inhibits thrombotic vessel occlusion in the mouse femoral artery and in vitro platelet aggregation. *Eur J Pharmacol* 2002; 455: 53–7.
38. Dent SB, Peterson CT, Brace LD, Swain JH, Reddy MB, Hanson KB, et al. Soy protein intake by perimenopausal women does not affect circulating lipids and lipoproteins or coagulation and fibrinolytic factors. *J Nutr* 2001; 131: 2280–7.
39. Yang G, Shu XO, Jin F, Zhang X, Li HL, Li Q, Gao YT, Zheng W. Longitudinal study of soy food intake and blood pressure among middle–aged and elderly Chinese women. *Am J Clin Nutr* 2005; 81: 1012–7.