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The Effects of Low Calorie Diet with Soy Protein on Cardiovascular Risk Factors in Hyperlipidemic Patients

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Abstract: Serum lipid abnormalities are an established risk factor for cardiovascular disease in hyperlipidemic patients. Because of the side effect of long-term medications in these patients, soy protein, as a part of healthy diet, may improve their lipid profile. The purpose of this study was to determine the effect of soy protein with low-calorie diet on lipid profiles in hyperlipidemic patient. Fifty two hyperlipidemic patients of both sex and age range of 25-65 years were participated. The patients received low-calorie diet based on 1400 kcal energy 18% protein, 24% fat and 58% carbohydrate per day for 4 weeks. The treatment group received low-calorie diet including (30 g day^{-1}) of soy protein. Blood samples were obtained after an overnight (12 h) fasting period before the study and in the last day of the intervention period. Anthropometric indices and levels of serum triacylglycerol, total cholesterol, low-density lipoprotein and high-density lipoprotein were measured before and after the intervention. In groups, weight, body mass index, waist and hip circumferences were significantly reduced ($p<0.05$) after four weeks. In comparison with control group, the results of treatment of soy protein with low-calorie diet showed that at the end of 4th week serum low-density lipoprotein was significantly ($p<0.05$) decreased while an insignificant reduction was seen in total cholesterol. This study suggest that soy protein with low calorie diet for 4 weeks treatment may be safe and effective alternative therapy for diminished the cardiovascular risk factors in hyperlipidemic patients.

Key words: Diet, soy protein, low density lipoprotein, high density lipoprotein, total cholesterol

INTRODUCTION

The morbidity and mortality associated with Cardio Vascular Disease (CVD) make it a major public health problem. Mortality from all heart disease increases with age in all races and both sexes (Thom *et al*., 2006). The importance of non-pharmacological control of plasma lipids is increasing along with the number of subjects whose plasma lipid levels are non-optimal. Consumption of soy protein as a nutritional intervention may prevent cardiovascular disease (Poli *et al*., 2008).

Soybeans contain all of the essential amino acids necessary for human nutrition and have been grown harvested for thousands of years. Soy is well tolerated and because it is a complete source of protein (Wansink and Cheong, 2002), can be substitution for higher-fat animal products (Michelfelder, 2009). Consumption of a diet with soy protein induced a decrease in the plasma level of Total Cholesterol (TC) and Low-Density Lipoprotein (LDL) in hypercholestrolemic subjects (Hoie *et al*., 2005; Blachier *et al*., 2010), in obese adults (Liao *et al*., 2007) in hyperlipidemic postmenopausal women (Shidfar *et al*., 2009; Hanachi and Golkho, 2008) and also in rat model (Oboh, 2006; Anosike *et al*., 2008) but there was no significant effect on plasma triacylglycerols (TAG) (Teixeira *et al*., 2000; Hoie *et al*., 2005). However, a 24 weeks, diet supplemented with soy protein in hypercholesterolemic subjects showed no significant changes in plasma TC, LDL and TAG (Dent *et al*., 2001; Hermansen *et al*., 2005). Moreover, in a recent study in mildly hypercholestrolemic subjects, a dietary intervention of soy protein for ten weeks was reported had no significant effects on LDL and high-density lipoprotein (HDL) (Thorp *et al*., 2008).

Result from different studies on the effect of soy protein on lipid profile is inconsistent and there are few data focusing on the effect of soy protein with a low-calorie diet on blood lipids in hyperlipidemic patients. Hence, the objective of this study was to investigate the effect of soy protein with low-calorie diet on blood lipids TAG, TC, LDL and HDL in hyperlipidemic patients.

Since, for primary prevention of coronary artery disease, physicians and patients often wish to avoid pharmacologic therapy of elevated cholesterol

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concentrations. The use of adjuncts to diet such as soy protein may allow target lipid concentrations to be reached without the use of drugs.

MATERIALS AND METHODS

Patients: This randomized clinical trial was conducted on 52 hyperlipidemic patients who were healthy in other respects and were recruited from nutrition and diet therapy clinic in Boalisina Hospital, Qazvin University of Medical Science, Iran in 2010. The inclusion criteria required the age of 25-65 years. The inclusion criteria required all subjects were between 25-65 years old. They had at least one of blood lipid indices including TC≥200, HDL≤40, LDL≥130 and TAG≥150 mg dL^{-1}. Exclusion criteria included pregnancy and lactation, smoking, steroid therapy, taking lipid-lowering drugs, hormone and a personal history of nephropathy, cardiovascular disease, diabetes and other chronic disease.

Protocol: Fifty-two subjects (45 female and 7 male) participated in this study. They were randomly divided into treatment (n = 26) and control (n = 26) groups. All subjects received a low calorie diet based on 1400 kcal energy per day for 4 weeks, including 24% fat, 18% proteins and 58% carbohydrate from registered dietitian.

Treatment group received the low-calorie diet including (30 g day^{-1}) soy protein. Soy protein was prepared by Shaddasht Soy Protein Company, Qazvin, Iran. The soy protein was used had national quality control certificate number 4935. The low calorie diet with soy protein was well tolerated and accepted overall cases. Oral and written instructions for recording foods were given to all subjects by the clinical nutritionist.

Seven-day food records and main daily nutrient intake record, completed during the last week of the study by subjects. All these records were reviewed by the clinical nutritionist for checking the diet compliance. Subjects´ compliance was assessed by analysing seven days diet records and was analyzed by using a computerized nutrient database (Dorosty Food Processor-DFP, version 2003, Shahid Beheshti University, Tehran, Iran), which is mainly based on the national nutrient composition data. Blood samples were obtained after an overnight (12 h) fasting period before the study and in the last day of the intervention period. Anthropometric indices and levels of serum TAG, TC, LDL and HDL were measured before and after the intervention. Serum total cholesterol and triacylglycerol concentration were measured by commercially available enzymatic reagents (Pars Azmoon, Tehran, Iran) adopted to Selectra autoanalyzer (Vital Scientific, Spankeren, Netherlands). HDL-cholesterol was measured after precipitation of the apolipoprotein B containing lipoproteins with phosphotungistic acids (Burstein *et al.*, 1970). Inter- and intra-assay coefficients of variation were both less than 5% for all these measurements.

Measurements: Body weight was measured with minimally clothed, without shoes with Digital scales. Height was measured in a standing position, without shoes, using a tape meter while the shoulders were in a normal state. Waist circumference was measured to the nearest 0.1 cm at the narrowest level over light clothing, using an unstretched tape measure. During the study, participants were asked not to change their habitual physical activity levels. All patients gave informed consent for their participation in the study after reading the protocol of this experiment and receiving information about soy protein consumption. The study protocol was approved by the Research Council and Ethical Committee of Qazvin University of Medical Sciences.

Statistical analyses: Results are presented as Mean±Standard deviation. Data were analyzed with the SPSS Statistical analysis software and t-test was used for analysis of differences between the groups. Paired t-test was applied to determine the difference between before and after measurements. One sample t-test for decreasing of blood lipids. A probability value of $p<0.05$ was accepted as statistically significant for all tests. The reduction percent of blood lipids after intervention was calculated as:

$$\%\,\text{reduction (loss)} = 100 \times (X_1 - X_2) / X_1$$

where, X_1 is blood lipids before intervention and X_2 is blood lipids after intervention.

RESULTS

The mean age of subjects was 38.90±8.79 years and the average of weight, waist and hip were 85.87 ±14.42 kg, 107.60±15.04 cm and 113.62±10.54 cm, respectively. Body mass index (BMI) and waist-to-hip ratio (WHR) were 33.08±5.32 kg m^{-2} and 0.94±0.07, respectively (Table 1). Body mass index and waist-to-hip ratio in the treatment groups were 32.73±5.90 k g m^{-2} vs. 33.42±5.33 kg m^{-2} and 0.94±0.08 vs 0.95±0.07 at baseline, repectively (Table 2). There were no significant differences in age, weight, height, waist, hip, BMI, WHR, TC, TAG, LDL, HDL, LDL/HDL and Chol/HDL between the two groups (treatment and control) at the baseline). Total cholesterol and LDL in the treatment and the control groups were 216.69±28.91 mg dL^{-1} vs 228.50±30.87 mg dL^{-1} and 129.29±22.22 mg dL^{-1} vs. 135.98±28.47 mg dL^{-1} at baseline, respectively. Weight, BMI, waist and hip circumferences were significantly reduced ($p<0.05$) after

4 weeks in both groups (Table 3). There were no significant differences at the beginning of dietary intervention (baseline) between plasma lipid concentrations. A low-calorie diet including soy protein intervention resulted in significantly lower levels of LDL than baseline 129.29±22.22 mg dL^{-1} versus 111.81±20.92 mg dL^{-1}, ($p<0.05$). Soy protein with low-calorie diet was associated with a significant reduction in serum LDL ($p<0.05$). Intervention diet significantly decreased Total cholesterol and Triacylglycerol compared with the baseline 216.69±28.91 mg dL^{-1} versus 187.79±27.53 mg dL^{-1} and 205.73±138.18 mg dL^{-1}versus 168.69±136.40 mg dL^{-1}, respectively ($p<0.05$) but compared with the control group, these changes were insignificant. No significant change occurred in HDL, LDL/HDL and Chol/HDL. Lipid profile before and after intervention, in both groups, are summarized in Table 3.

Table 1: Characteristics of patients

Characteristics	Minimum	Maximum	(n)	Mean±SD
Age (years)	25.00	58.00	52	38.90±8.79
Weight (kg)	56.90	121.30	52	85.87±14.42
Height (cm)	148.00	190.00	52	161.19±7.91
Waist (cm)	78.00	144.00	51	107.60±15.04
Hip (cm)	93.00	143.00	51	113.62±10.54
BMI (kg m^{-2})	24.24	47.45	52	33.08±5.32
WHR (Ratio)	0.79	1.06	52	0.94±0.07
Calorie (kcal)	868.14	2286.00	51	1385.00±299.8
Carbohydrate (%)	44.00	75.90	52	57.90±6.5
Protein (%)	12.16	29.16	52	18.30±2.8
Fat (%)	13.40	37.00	52	26.10±5.4
Cholesterol (mg dL^{-1})	145.00	282.00	52	222.59±30.16
LDL (mg dL^{-1})	71.00	190.00	52	132.27±25.28
HDL (mg dL^{-1})	16.30	78.00	51	44.24±11.89
LDL/HDL	1.39	5.52	51	3.15±0.93
Chol/HDL	2.87	12.73	51	5.35±1.66

Values are Mean±SD; LDL: Low-density, lipoprotein; HDL: High-density lipoprotein; WHR: waist to hip ratio; BMI: Body mass index

Table 2: Baseline characteristics of patients

Characteristics	Treatment (n = 26)	Control (n = 26)	p-value
Age (year)	38.65±8.79	39.15±8.95	0.37
Weight (kg)	83.89±15.23	87.86±13.56	0.98
Height(cm)	160.08±8.36	162.31±7.44	0.30
Waist (cm)	105.84±14.72	109.31±15.45	0.59
Hip (cm)	112.32±9.79	114.89±11.26	0.39
BMI (kg m^{-2})	32.73±5.40	33.42±5.33	0.65
WHR (Ratio)	0.94±0.08	0.95±0.07	0.66
Calorie (kcal)	1399.8±346.7	1372.10±258.8	0.76
Carbohydrate (%)	59.3±7.40	56.70±5.50	0.19
Protein (%)	18.7±2.00	17.90±3.30	0.36
Fat (%)	24.6±5.70	27.50±4.80	0.07
Cholesterol (mg dL^{-1})	216.69±28.91	228.50±30.78	0.16
Triglyceride (mg dL^{-1})	205.73±138.18	195.08±67.10	0.73
LDL (mg dL^{-1})	129.29±22.22	135.98±28.47	0.40
HDL (mg dL^{-1})	43.82±12.56	44.68±11.39	0.80
LDL/HDL	3.14±0.87	3.18±1.03	0.91
Chol/HDL	5.37±1.95	5.34±1.35	0.96

Values are Mean±SD, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: WHR: waist to hip ratio, BMI: Body mass index

DISCUSSION

Treatment with diet including soy protein for 4 weeks resulted in a significant decrease in LDL cholesterol by 7.3%. However, insignificant change occurred in other lipid profile. More recently the INTERHEART case controlled study identified that more than 35% of heart attacks were due to abnormal blood lipids; those with abnormal blood lipids have a threefold risk of heart attack compared to those with normal levels (Yusuf *et al*., 2004). Consistent with our result, in a recent meta-analysis (Taku *et al*., 2007) of 11 randomized controlled trials published from 1990 to 2006 described no significant changes in HDL cholesterol and triacyglycerol were found after consumption of soy protein. In several studies, similar to the result of this study, soy protein did not show any significant increase in blood HDL (Ma *et al*., 2005; Hoie *et al*., 2005; Sacks *et al*., 2006; Thorp *et al*., 2008; Xiao, 2008). Also in a rat model Reza *et al.* (2008) indicated that at the end of 7th week feeding dietary soybean, unchanged level of HDL was seen. However, Anderson *et al*. (1995) and Weggemans and Trautwein (2003) found increasing in HDL cholesterol after intake of soy protein.

Table 3: Characteristics of 52 hyperlipidemic patients before and after intervention

	Treatment group (n = 26)		Control group (n = 26)	
Characteristics	After	Before	After	Before
Cholesterol (mg dL^{-1})	216.69±28.91	187.79±27.53*	228.50±30.78	203.89±30.45*
Triacylglycerol (mg dL^{-1})	205.73±138.18	168.69±136.40*	195.08±67.10	161.27±60.85*
LDL (mg dL^{-1})	129.29±22.22	111.81± 20.92*	135.98±28.47	125.40±19.20
HDL (mg dL^{-1})	43.82±12.56	40.47±12.67	44.68±11.39	39.88±8.30
LDL/HDL	3.14±0.87	2.98±0.97	3.18±1.03	3.21±0.76
Chol/HDL	5.37±1.95	5.13±2.15	5.34±1.35	5.20±1.10
Weight (kg)	83.89±15.24	80.471±15.13*	87.86±13.56	84.55±12.46*
Waist (Cm)	105.84±14.72	101.72±14.3*	109.31±15.45	104.46±14.87*
Hip (Cm)	112.32±4.79	109.08±9.53*	114.84±11.26	110.54±14.02*
Body Mass Index (kg m^{-2})	32.74±5.40	31.40±5.34*	33.42±5.33	32.17±4.48*
Waist to hip Ratio	0.94±0.07	0.93±0.07	0.95± 0.07	0.95±0.12

Values are Mean±SD, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SD: WHR: waist to hip ratio, BMI: Body mass index, * Significantly at $p<0.05$

Zhan and Ho (2005) reported improvements in HDL cholesterol after soy protein consumption were only observed in studies of >12 week duration. It seems that 4 week treatment period of current study was brief for increasing the HDL level. In the present study, LDL cholesterol was reduced 7.3% in the group that consumed soy protein. However, Dent *et al.* (2001) and Ma *et al.* (2005) found no effect of soy protein treatment on circulating LDL cholesterol may be due to more valuable baseline LDL values. Over a period of 5 years, each 1% decline in LDL cholesterol is associated with a reduction of ~1% CVD event risk and if maintained during a longer period of time, CVD event risk reduction may be as much as 3% for each 1% reduction in LDL cholesterol (Brown *et al.*, 2006). Harland and Haffner (2008) observed that the modest amounts of soy protein (25 g) in to the diet of adult with normal or mild hypercholesterolaemic resulted in significant (6%) reduction in LDL cholesterol. Furthermore, Jenkins *et al.* (2010), Bruckert and Rosenbaum (2011) and Hansel *et al.* (2011) also reported a 3-10% reduction in blood LDL using soy protein, which support the results of the current study. The effect of LDL reduction by soy protein consumption has benefit for CHD prevention. A decrease of 1 mg dL^{-1} in LDL cholesterol results in about a 1 to 2% decrease in the factor for CHD (Lichtenstein *et al.*, 2006). Soybeans contain 2 types of storage protein, the globulins 11 S and 7 S. Cell culture studies suggest that these globulins stimulate LDL receptor activity (Lovati *et al.*, 1992). The result of more recent study on rats also showed that the oral daily administration of soybean 7 S globulin in the diet to hypercholesterolemic rats promotes the reduction of LDL cholesterol (Ferreira *et al.*, 2011). The results of this study showed an insignificant reduction in total cholesterol. In 29 controlled studies (Anderson *et al.*, 1995), a trend emerged that soy protein selectively reduced blood cholesterol in direct proportion to the degree of hypercholesterolemia. In hyperlipidemic patients with initial blood cholesterol was <255 mg dL^{-1}, similar to the present study, there was no significant reduction in blood cholesterol by soy protein (Sacks *et al.*, 2006). Thus the response to soy protein was determined by the initial blood cholesterol level.

The range of soy protein that was used in previous studies was 25 to 135 g d^{-1}; the range for isoflavones was 40 to 318 mg (Sacks *et al.*, 2006). In the present study, the soy protein was used contained 1.5 mg isoflavones/g protein. The isoflavone content of soy products has been hypothesized to contribute to their LDL lowering effects. (Zhan and Ho, 2005; Xiao, 2008; Messina, 2008; Blachier *et al.*, 2010) similar to the result of the present study.

However, other well-controlled studies did not find significant effects of soy isoflavones on LDL cholesterol (Weggemans and Trautwein, 2003; Kreijkamp-Kaspers *et al.*, 2004; Zittermann *et al.*, 2004; McVeigh *et al.*, 2006; Taku *et al.*, 2007, 2008; Thorp *et al.*, 2008; Campbell *et al.*, 2010; Maki *et al.*, 2010). The mechanisms responsible for the effect of soy isoflavones on the lipid are still being explored.

In some intervention studies, 3 days food record has been used (Hermansen *et al.*, 2005) to reach a more accurate energy estimation and macronutrients intake; the subjects of this study were asked to record their food for one week.

In conclusion, the results of the present study showed that short-term consumption of soy protein with a low calorie diet as a part of healthy diet lowered the serum LDL cholesterol level. This effect is beneficial and may reduce the cardiovascular risk factor in hyperlepidemic patients and postponement of the requirement for drug therapy for these patients.

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REFERANCES

Anderson, J.W., B.M. Johnstone and M.E. Cook-Newell, 1995. Meta-analysis of the effects of soy protein intake on serum lipids. N. Engl. J. Med., 333: 276-282.

Anosike, C.A., O. Obidoa and L.U.S. Ezeanyika, 2008. Beneficial effects of soybean diet on serum marker enzymes, lipid profile and relative organ weights of wistar rats. Pak. J. Nutr., 7: 817-822.

Blachier, F., A.H. Lancha, C. Boutry and D. Tome, 2010. Alimentary proteins, amino acids and cholesterolemia. Amino Acids, 38: 15-22.

Brown, B.G., K.H. Stukovsky and X.Q. Zhao, 2006. Simultaneous low-density lipoprotein-C lowering and high-density lipoprotein-C elevation for optimum cardiovascular disease prevention with various drug classes, and their combinations: A meta-analysis of 23 randomized lipid trials. Curr. Opin. Lipidol., 17: 631-636.

Bruckert, E. and D. Rosenbaum, 2011. Lowering LDL-cholesterol through diet: Potential role in the statin era. Curr. Opin. Lipidol., 22: 43-48.

Burstein, M., H.R. Scholnic and R. Morfin, 1970. Rapid method for the isolation of lipoproteins from human serum by precipitation with poly amion. J. Lipid Res., 11: 583-595.

Campbell, S.C., D.A. Khalil, M.E. Payton and B.H. Arjmandi, 2010. One-year soy protein supplementation does not improve lipid profile in postmenopausal women. Menopause, 17: 587-593.

Dent, S.B., C.T. Peterson, L.D. Brace, J.H. Swain and M.B. Reddy *et al*., 2001. Soy protein intake by perimenopausal women does not affect circulating lipids and lipoproteins or coagulation and fibrinolytic factors. J. Nutr., 131: 2280-2287.

Ferreira, E.S., M.A. Silva, A. Demonte and V.A. Neves, 2011. Soy α-conglycinin (7s globulin) reduces plasma and liver cholesterol in rats fed hypercholesterolemic diet. J. Med. Food, 14: 94-100.

Hanachi, P. and S. Golkho, 2008. Assessment of soy phytoestrogens and exercise on lipid profiles and menopause symptoms in menopausal women. J. Boil. Sci., 8: 789-793.

Hansel, B., R. Courie, Y. Bayet, F. Delestre and E. Bruckert, 2011. Phytosterols and atherosclerosis. Rev. Med. Internet, 32: 124-129.

Harland, J.I. and T.A. Haffner, 2008. Systematic review, meta-analysis and regression of randomised controlled trials reporting an association between an intake of circa 25 g soya protein per day and blood cholesterol. Atherosclerosis, 200: 13-27.

Hermansen, K., B. Hansen, R. Jacobsen, P. Clausen and M. Dalgaard *et al*., 2005. Effects of soy supplementation on blood lipids and arterial function in hypercholesterolaemic subjects. Eur. J. Clin. Nutr., 59: 843-850.

Hoie, L.H., H.J. Graubaum, A. Harde, J. Gruenwald and K.D. Wernecke, 2005. Lipid-lowering effect of 2 dosages of a soy protein supplement in hypercholesterolemia. Adv. Ther., 22: 175-186.

Jenkins, D.J., A. Mirrahimi, K. Srichaikul, C.E. Berryman and L. Wang *et al*., 2010. Soy protein reduces serum cholesterol by both intrinsic and food displacement mechamisms. J. Nutr., 140: 2302S-2311S.

Kreijkamp-Kaspers, S., L. Kok, D.E. Grobbee, E.H. de Haan, A. Aleman, J.W. Lampe and Y.T. van der Schouw, 2004. Effect of soy protein containing isoflavones on cognitive function, bone mineral density and plasma lipids in postmenopausal women: A randomized controlled trial. J. Am. Med. Assco., 292: 65-74.

Liao, F.H., M.J. Shieh, S.C. Yang, S.H. Lin and Y.W. Chien, 2007. Effectiveness of a soy-based compared with a traditional low-calorie diet on weight loss and lipid levels in overweight adults. Nutrition, 23: 551-556.

Lichtenstein, A.H., L.J. Appel, M. Brands, M. Carnethon and S. Daniels *et al*., 2006. Diet and lifestyle recommendations revision 2006: A scientific statement from the American Heart Association Nutrition Committee. Circulation, 114: 82-96.

Lovati, M.R., C. Manzoni, A. Corsini, A. Granata, R. Frattini, R. Fumagalli and C.R. Sirtori, 1992. Low density lipoprotein receptor activity is modulated by soybean globulins in cell culture. J. Nutr., 122: 1971-1978.

Ma, Y., D. Chiriboga, B.C. Olendzki, R. Nicolosi, P.A. Merriam and I.S. Ockene, 2005. Effect of soy protein containing isoflavones on blood lipids in moderately hypercholesterolemic adults: A randomized controlled trial. J. Am. Coll. Nutr., 24: 275-285.

Maki, K.C., D.N. Butteiger, T.M. Rains, A. Lawless, M.S. Reeves, C. Schasteen and E.S. Krul, 2010. Effects of soy protein on lipoprotein lipids and fecal bile acid excretion in men and women with moderate hypercholesterolemia. J. Clin. Lipidol., 4: 531-542.

McVeigh, B.L., B.L. Dillingham, J.W. Lampe and A.M. Duncan, 2006. Effect of soy protein varying in isoflavone content on serum lipids in health young me. Am. J. Clin. Nutr., 83: 244-251.

Messina, M., 2008. Investigating the optimal soy protein and isoflavone intakes for women: A perspective. Women's Health (London England), 4: 337-356.

Michelfelder, A.J., 2009. Soy: A complete source of protein. Am. Fam. Physician, 79: 43-47.

Oboh, G., 2006. Coagulants modulate the antioxidant properties and hypocholesterolemic effect of Tofu (Curdled Soymilk). Asian J. Biochem., 1: 57-66.

Poli, A., F. Marangoni, R. Paoletti, E. Mannarino and G. Lupattelli *et al*., 2008. Non-pharmacological control of plasma cholesterol levels. Nutr. Metab. Cardiovasc. Dis., 18: S1-16.

Reza, N.M., B.R. Fatemeh, M.T. Fahimeh, G.N. Fatemeh and B.R. Morteza, 2008. Hypocholesterolemic effects of dietary soybean vs. casein proteins in a crossed over diets in rat. Pak. J. Biol. Sci., 11: 1467-1471.

Sacks, F.M., A. Lichtenstein, L. Van Horn, W. Harris, P. Kris-Etherton and M. Winston, 2006. American heart association nutrition committee1, Soy protein, isoflavones, and cardiovascular health: An American heart association science advisory for professionals from the nutrition committee. Circulation, 113: 1034-1044.

Shidfar, F., E. Ehramphosh, I. Heydari, L. Haghighi, S. Hosseini and S. Shidfar, 2009. Effects of soy bean on serum paraoxonase 1 activity and lipoproteins in hyperlipidemic postmenopausal women. Int. J. Food Sci. Nutr., 60: 195-205.

Taku, K., K. Umegaki, Y. Sato, Y. Taki, K. Endoh and S. Watanabe, 2007. Soy isoflavones lower serum total and LDL cholesterol in humans: A meta-analysis of 11 randomized controlled trials. Am. J. Clin. Nutr., 85: 1148-1156.

Taku, K., K. Umegaki, Y. Ishimi and S. Watanabe, 2008. Effects of extracted soy isoflavones alone on blood total and LDL cholesterol: Meta-analysis of randomized controlled trials. Ther. Clin. Risk Manage., 4: 1097-1103.

Teixeira, S.R., S.M. Potter, R. Weigel, S. Hannum, J.W. Jr. Erdman and C.M. Hasler, 2000. Effects of feeding 4 levels of soy protein for 3 and 6 weeks on blood lipids and apolipoproteins in moderately hypercholesterolemic men. Am. J. Clin. Nutr., 71: 1077-1084.

Thom, T., N. Haase, W. Rosamond, V.J. Howard and J. Rumsfeld *et al*., 2006. Heart disease and stroke statistics-2006 update: A report from the American heart association statistics committee and stroke statistics subcommittee. Circulation, 113: e85-e151.

Thorp, A.A., P.R. Howe, T.A. Mori, A.M. Coates and J.D. Buckley *et al*., 2008. Soy food consumption does not lower LDL cholesterol in either equol or nonequol producers. Am. J. Clin. Nutr., 88: 298-304.

Wansink, B. and J. Cheong, 2002. Taste profiles that correlate with soy consumption in developing countries. Pak. J. Nutr., 1: 276-278.

Weggemans, R.M. and E.A. Trautwein, 2003. Relation between soy associated isoflavones and LDL and HDL cholesterol concentrations in humans: A meta-analysis. Eur. J. Clin. Nutr., 57: 940-946.

Xiao, C.W., 2008. Health effects of soy protein and isoflavones in humans. J. Nutr., 138: 1244S-1249S.

Yusuf, S., S. Hawken, S. Ounpuu, T. Dans and A. Avezum *et al*., 2004. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. Lancet, 364: 937-952.

Zhan, S. and S.C. Ho, 2005. Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. Am. J. Clin. Nutr., 81: 397-408.

Zittermann, A., J. Geppert, S. Baier, N. Zehn and I. Gouni-Berthold *et al*., 2004. Short-term effects of high soy supplementation on sex hormones, bone markers, and lipid parameters in young female adults. Eur. J. Nutr., 43: 100-108.