BENEFICIAL EFFECTS OF SOYPROTEIN ISOFLAVONES ON LIPID AND BLOOD GLUCOSE CONCENTRATIONS IN TYPE 2 DIABETIC SUBJECTS

Shahbazian H.B.[*], Amani R. [**], Siadatan J., Shahbazian H.[*], Latifi M. [***], Ahmadzadeh A.[*] and Haghighizadeh M. [***]

**Endocrine Department, Golestan Hospital, Ahwaz Jundishapur University of Medical Sciences*
***School of Paramedical Sciences, Ahwaz Jundishapur University of Medical Sciences*
****School of Health, Ahwaz Jundishapur University of Medical Sciences*
Accepted: *23th Nov. 2005* ***Received:*** *10th Feb. 2006*

Abstract

Consumption of soyprotein has recently been shown to improve the blood lipid levels in non-diabetic subjects. The purpose of this study was to evaluate if a dietary soyprotein isoflavones affects lipid and blood glucose levels in type 2 diabetic subjects. Twenty six type 2 diabetic patients who had refferd to Ahvaz Jundishapour University Diabetes Center, due to uncontrolled diabetes, participated in this study. They completed a trial of dietary supplementation with 25gr/day of a processed defeated meal containing 12 gr soyprotein and about 50mg isoflavones, for 3 months. FBS, HbA1C, serum total cholesterol, triglyceride, HDL and LDL-C and patients, weight and blood pressure were checked before soyprotein consumption and monthly thereafter. There were significant differences in mean FBS (153±50 versus 178±60, P< 0.015), HbA1C (8.8 ± 1.4 versus 9.6 ± 1.7 percent, P<0.001), triglycerides concentration (229 ± 113 versus 267 ± 149 P<0.008) and total cholesterol (196 ± 41 versus 207 ± 42, P<0.002) before and after three months consumption of soyprotein isoflavones.There were no significant changes in HDL and LDL-C cholesterol levels, blood pressure and weight.

Key words:

Blood glucose, Diabetes type 2, Soyprotein and isoflavones, Blood lipids.

Introduction

Evidence is emerging that dietary supplementation with soyprotein has a beneficial role in type 2 diabetes (1,2). Nutritional intervention studies performed in animals and humans suggest that the ingestion of soyprotein with isoflavones and flaxseed rich in lignans improves glucose control and insulin resistance (3,4). In animal models of obesity and diabetes, soyprotein has been shown to reduce serum insulin and insulin resistance (2,5,6,7). In studies of human subjects with or without diabetes soyprotein also appears to improve hyperglycemia and reduce body weight, hyperlipidemia and hyperinsulinemia and sporting its beneficial effects on obesity and diabetes (1,2,8,9,10,11,12).

A meta-analysis of 38 controlled clinical trials indicated that soyprotein was effective in lowering plasma cholesterol, LDL cholesterol, and triglycerides concentrations (13). In a small acute study, supplementation of soy fibers for obese type 2 diabetic subjects also seemed to reduce the rise of postprandial plasma triglycerides and mildly lower the blood glucose response without affecting the insulin levels (10). This raises the question if soy products may improve the glycemic control in type 2 diabetic subjects. The purpose of the present study was to assess the effects of a 25g defalted meal contain soyprotein (48gr/100gr) and isoflavones (195mg/100gr) taken one time daily as a

[*]Email: Hjb_shahbazian@yahoo.com

beverage with regular meals for 3 months, on serum levels of total cholesterol, triglycerides, HDL-C, LDL-C, FBS, HbA1C, patient weight and blood pressure.

Materials and methods

Twenty six type 2 diabetic subjects who had refferd to Ahvaz Jundishapour University Diabetes Center for uncontrolled diabetes, completed the study. Eleven patients had previous history of hypertension and 3 of microalbuminuria. All of patients were treated with diet and anti diabetic drugs (18 sulfonylureas, 11 metformin, 4 combined sulfonylureas and metformin and 1 insulin). They took the prescribed medicine throughout the study without any changes. Subjects were asked to maintain their habitual diet and level of physical activity and all were in good general health and had a normal renal function. Informed written consent was obtained from each subject. All subjects received 25gr/day defeated soyprotein meal providing a daily amount of 12gr soyprotein with about 50mg isoflavones for three months. Subjects were instructed to mix their daily supplement in 200ml water and consume as a beverage with their current meals. The participants were weighed monthly. Blood samples for measuring FBS, HbA1C, total cholesterol, TG and HDL-C were obtained after an overnight fasting period before the study and monthly thereafter. LDL cholesterol was calculated using the Friedwald equation. Blood pressure was measured before study and at each monthly visit. Plasma glucose concentration were measured by the glucose oxidase method and HbA1C by HPLC. Serum Triglyceride, total cholesterol and HDL-C were measured using Pars Azemon kits on a RA-XY and RA-1000 Automatic Analyzer. Statistical analysis was performed using SPSS soft-ware 11.5 version. Significant point was set at 0.05 level.

Results

A total of 26 (17 female and 9 male) type 2 diabetic patients completed the study. Soy preparation was well tolerated. Patients age were between 39 to 70 years (mean: 24 ± 8.4 years). Mean time from diagnosis of type 2 diabetes was 6.5 ± 4.3 years (between one month to 15 years). FBS and HbA1C levels decreased significantly after three months consumption of the soyproduct. (152 ± 50 versus 178 ± 60 and 8.8±1.4 versus 9.6±1.7 percent respectively). Although serum total cholesterol and TG concentrations decreased significantly after three months ($P<0.002$ & <0.008, respectively), there were no significant differences in LDL and HDL cholesterol levels (Table 1). Systolic and diastolic blood pressure and patients weights remained unchanged during the study. Only FBS levels showed significant changes in first and second months after consumption of soyproduct. ($P<0.03$ & $P<0.02$, respectively).

Table 1: Blood glucose, lipids and blood pressure before, during and after three months consumption of soy product.

Variables	Before study	After 1 months	After 2 months	After 3 months	P value (3th month versus baseline)
FBS(mg/dl)	178 ± 69	16 ± 63	157 ± 53	152 ± 50	0.015
HbA1c %	9.6 ± 1.7	9.3 ± 1.5	9 ± 1.3	8.8 ± 1.4	<0.001
LDL(mg/dl)	114 ± 38	112 ± 35	114 ± 38	110 ± 37	0.076
HDL(mg/dl)	46 ± 6	44 ± 6	45 ± 5	45 ± 5	0.27
TG(mg/dl)	267 ± 149	261 ± 146	243 ± 122	229 ± 113	0.008
Chol(mg/dl)	207 ± 42	203 ± 40	203 ± 40	196 ± 41	0.002
Systolic BP(mmHg)	138 ± 31	132 ± 23	131 ± 18	130.96	0.101
Diastolic BP(mmHg)	87 ± 20	84 ± 16	84 ± 15	84 ± 16	0.384

Discussion

The soyprotein isoflavones (SPI) used in this study reduced FBS by 15%, HbA1C by 7%, Triglycerides by 14% and total cholesterol concentrations by 5%. The results showed that soy supplementation has a significant effect on both glycemic control and lipid profile in type 2 diabetes patients. The therapeutic potential of soy for diabetes was first suggested in 1910 (14). The few small studies of the effect of soy on glycemic control in diabetes have shown inconsistent results that have been primarily attributed to the soluble fiber content of soy bean preparation (10,11,12). In a study of 14 women and 6 men, 6 weeks of treatment with soyprotein (50gr/day), isoflavones (165mg/day), and cotyledon fiber (20gr/day) compared with placebo (casein 50gr/day and cellulose 20gr/day) showed an improvement in lipid parameters but no difference in glucose, insulin, or HbA1C (1). A cross-over trial of soy phytoestrgen (soyprotein 30 gr/day, isoflavones 132mg/day versus placebo) intake in 32 postmenopausal women with type 2 diabetes for 2 weeks (with a 2 weeks washout period) showed a significant decrease in insulin resistance, HbA1C, total cholesterol, LDL cholesterol and cholesterol/HDL ratio, but no significant changes in HDL cholesterol, Triglycerides, weight and blood pressure (2). In this study similar results were obtained regarding fasting blood glucose, HbA1C, total cholesterol, HDL-C, blood pressure and weight, however LDL-C showed no significant decrease.

A modest improvement in blood glucose attributed to fiber intake from soy beans has been reported previously in individuals with type 2 diabetes, in both short and longer studies (10,11). In vitro studies suggested several mechanisms for a direct pharmacological action of soy on glycemic control, including a tyrosine kinase inhibitory action, changes in insulin receptor numbers and affinity, intracellular phoshorylation and alterations in glucose transport (15,16,17,18). In this study decreases in both FBS and HbA1C without any changes in patient's weight seems to support a direct favorable effect of soy in these patients. The mechanisms for the lipid lowering effect of soy products are not known. There is persuasive evidence to implicate soy protein in the cholesterol-lowering effect. Soyprotein provide a large amount of protein with high-quality amino acids, which seems to upregulate LDL receptors directly by 50% or more (19). The question of the mechanism involved is important, because selection of the protein source plays a critical role in the development of products with a greater or lesser likelihood of reducing serum cholesterol in humans. There is abundant evidence that both purified viscous soluble fiber and soluble fiber in foods reduce serum cholesterol levels (20). The action of soluble fiber seems to relate to an increase in fecal bile acid loss (21). The dietary soluble fiber in large amounts can result in a modest decrease in total and LDL cholesterol without changing HDL cholesterol also in people with diabetes, has been demonstrated in several studies (22,23). The meta analysis of Anderson et al (13), however, indicated that a considerable proportion of the effect of soy products on serum cholesterol might be linked to the effects of isoflavones. Since isoflavones are compounds that have structure similar to estrogens and bind to estrogen receptors, it has been postulated that this may be responsible for the effects of soyprotein on serum lipids (24). Two proposed mechanisms for a hypocholestrolemic effect of isoflavones are the up-regulation of LDL receptors and inhibition of endogenous cholesterol synthesis. A reduction in total cholesterol has been observed after consumption of 45mg isoflavones/day relative to levels during a control period with isoflavones-free products (24). In conclusion, these

results indicate beneficial effects of dietary supplementation with soy product on blood glucose and lipid profile of these type 2 diabetic patients. Thus a dietary supplementation with soy products in type 2 diabetic patients may provide an acceptable and effective option for blood glucose and lipid control there by decreasing the requirement for drug therapy in these patients.

Conclusion

The results indicate the beneficial effects of dietary supplementation with soyprotein and isoflavones on blood lipoproteins, and blood sugar levels, in type 2 diabetic subjects.

Acknowlegement

Special thanks to dector Ahmad Zand Moghadam for laboratory analysis of the soy product.

References

1) Hermansen K, Sendergaard M, Hoie L, Carstensen M, Brock B. Beneficial effects of a soy -based dietary supplement on lipid levels and cardivascular risk markers in type 2 diabetes subjects. Diabetes care 2001; 24: 228-233.

2) Jayagodal V, Albertazzi P, Kilpatric E.S, Howarth E.M, Jenniys P.E. Hepburn D.A, Atkin S.L. Beneficial effects of soy phytoestrogen intake in postmeno pausal women with type 2 diabetes. Diabetes care, 2002; 25: 1709-1714.

3) Bhathena S.J, Velasquez M.T. Beneficial role of dietary phytoestrogens in obesity and diabetes. Am Journal Clin Nutr, 2002; Vol. 76, No.6, 1991.1201.

4) Critani N, Sugimoto 7, Fukuda H, Komiya M, Ikeda H. Dietary soy been protein increase insulin receptor gen expresion in wistar fatty rats when dietary polyunsaturated fatty acid level is low. The Journal of Nutrition. 1997; Vol. 127 No.6: 1077-1083.

5) Hurleyc, Galibois I, Jacqes H. Fasting and postprandial lipid and glucose metabolism are modulated by dietary proteins and carbohydrates: role of plasma insulin concentrations. J Nutr Biochem 1995; 6: 540-6.

6) Sugano M, Ishiwaki N, Nagata Y. Imazumi K. Effects or arginine and lysine addition to case in and soy been protein on serum lipids, apolipo proteins, insulin and glucagon in rats. Br J Nutr 1982; 48: 211-21.

7) Baba N, Rawan H, Van Itallie 7. Effects of casein versus soyprotein diets on body composition and serum lipid levels in adult rats. Nut Res 1992; 12: 279-88.

8) Amani R, Zand-Moghaddam A, Jalali MT, Hatamizadeh MA. Effects of soy isoflavones on lipid profiles and hormones of hypercholesterolemic men. Int J Endocrinal Metab (2): 29-39; 2004.

9) Teixeira SR, Tappenden KA, Carson L, Jones R, Prabhudasai M, Mashall WP, Erdumun JW. Isolated soyprotein consumption reduces urinary albumin excretion and improves the serum lipid profile in men with type 2 diabetes mellitus and nephropathy.

10) Tsai AC, Vinik AI, Lasichll A, Loas: effects of soy polysaccharide on postprandial plasma glucose, insulin, glucagon, pancreatic polypeptide, somatostatin, and triglyceride in obese diabetic patients. Am J Clin Nutr 1987; 45: 596-601.

11) Mahalko JR, Sandstead HH, Johnson LK, Inman LF, Milne DB, Werner RC, Haunz EA: Effect of consuming fiber from corn bran, soy hulls, or apple powder on glucose tolerance and plasma lipids in type 2 diabetes. Am J Clin Nutr 1984; 39: 25-34.

12) Thomas BL, Laine DC, Goetz FC: Glucose and insulin response in diabetic subjects: acute effect of carbohydrate level and the addition of soy polysaccharide in defined formula diets. Am J Nutr 1998; 48: 1048-1052.

13) Anderson JW, Johnstone BM, Cook-Newell ME. Meta-analysis of the effect of soy protein intake on serum lipids. N Eng J Med 1995; 333: 276-282.

14) Friedwald J, Ruhrah J. The use of the soy been as a food in diabetes. Am J Med Sci 1910; 140: 793-803.

15) Vaavanam K, Srijayantas O, Reilly J, Raman A, Wisoman H. Antioxidant action and potential anidiabetic propreties of an isoflavonoid – containing soy abean phytochemical extract (SPE). Phytother Res 1999; 13: 601-608.

16) Sorenson RL, Brelje TC, Roth C. Effects of tyrosine kinase inhibitors on islets of langerhans. Endocrinology 1994; 134: 1975-1978.

17) Jonas JC, Plant TD, Gilon P, Detimary P, Nenguin M, Henguin JC: Multiple Effects of stimulation of insulin secretion by the tyrosine kinase inhibitor genistein in normal mouse islets. Br J phormacol 1995; 114: 872-880.

18) Abler A, Smith JA, Randatto PA, Rothenbers PL, Jarett L. Genistein differentially inhibits postrecoptor effects of insulin in rat adipocytes without inhibiting the isulin receptor kinase. J Biol Chem 1992; 267: 3946-3951.

19) Sirtori CR, Lovati MR, Manzoni C, Gianazza E, Bondioli A, Staels B, Auwerx J: Reductions of serum cholesterol by soy proteins: clinical experience and poteintial molecular mechanisms. Nutr Metab Cardiovasc Dis 1998; 8: 334-340.

20) Anderson JW, Garrity TF, Wood CL, Whitis SE, Smith BM, Oeltgen PR: Prospective, randomized, controlled comparisons of the effects of low-fat and low-fat plus high-fiber diets on serum lipid concentrations. Am J Clin Nutr 1992; 56:887-894.

21) Lia A, Hallmans G, Sandberg AS, Sundberg B, Aman P, Anderson H: Oat beta-glucgon increases bile acid excretion and a fiber-rich barley fraction increases cholesterol excretion in ileostomy subjects. Am J Clin Nutr 1995; 62: 1245-1251.

22) Uusitupa M, Siitonen O, Savolainen K, Silvasti M, Penttila I, Parviainen M: Metabolic and nutritional effects of long-term use of guar in the treatment of noninsulin-dependent diabetes of poor metabolic control. Am J Clin Nutr 1989; 49: 345-351.

23) Nuttall EQ: Dietary fiber in the management of diabetes. Diabetes 1993; 42:503-508.

24) Tham DM, Gardner CD, Haskell WL: Potential health benefits of dietary phytoestrogens: a review of the clinical, epidemiological, and mechanistic evidence. J Clin Endocrinol Metab 1998; 83: 2223-2235.