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Beneficial Effects of Soy Isoflavones on Blood Pressure and Lipid Profile in Indian Postmenopausal Women

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Abstract

Background: The studies have suggested that dietary isoflavones intake in postmenopausal women had protective role against cardiovascular disease (CVD). **Objectives:** This study ascertained the effect of isoflavone in the form of soyflour on lipid profiles and blood pressure (BP) in postmenopausal women diagnosed with medium risk of CVD. **Materials and Methods:** It was a 16-week placebo controlled trial that was conducted on 60 postmenopausal women aged 45–55 years. Participants in the treatment group were provided with 40 g soyflour/day for 16 weeks. The participants in the control group were asked not to change their usual dietary habits and lifestyles and were instructed to avoid taking soybean and soybean products. The changes in BP and blood lipid profile were measured at baseline and at the end of the study. **Results:** There were non-significant differences in any of the variables between two groups at baseline. Biochemical results indicated the beneficial effect of intervention in significantly reducing systolic (6.28%) and diastolic (4.73%) BP of the treatment group. It also exhibited an effective role in significantly ($P < 0.05$) reducing the serum cholesterol (17.29%), triglyceride (22.22%), low density lipoprotein (24.53%), very low density lipoprotein (22.21%), and significantly increasing the high density lipoprotein (13.55%) in the treatment group. **Conclusion:** The study indicates that daily administration of 40g soyflour for 16 weeks improved the BP and lipid profile of postmenopausal subjects.

Keywords: Blood pressure, Intervention, Lipid profile, Menopause, Soyflour

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Introduction

Menopause is a natural part of every woman's life, a transition from reproductive to non-reproductive stage. Menopause is documented as the permanent cessation of menstruation for a period of 1 year, normally occurs between 45 and 55 years. According to the Indian Menopausal Society, average age of menopause of an Indian woman is 46.2 years and there are currently about 65 million Indian women over the age of 45 years affected with menopause-related health problems.[1] With increase in life expectancy, a woman spends more than one-third of her lifespan in menopausal state. Hence, menopausal health demands even higher priority in Indian scenario.

According to the WHO (2017) cardiovascular diseases (CVD) remain the top cause of global mortality with an estimated 17.9 million attributed deaths in 2016 (31% of global deaths).[2] CVD is the most common and lethal outcome of hypertension. Hypertension has been associated with increased risk of coronary artery disease and is an independent risk factor for cardiovascular and cerebrovascular diseases.[3] The relationship between blood pressure (BP) and CVD risk is continuous such that the higher the BP, the greater the chance of myocardial infarction, heart failure, stroke, and kidney disease.[4] For people aged 40–70 years, each increment of 20 mmHg in systolic BP or 10mmHg in diastolic BP doubles the risk of CVD for BPs of 115/75–185/115 mmHg. Results from the great Indian BP survey revealed that the overall prevalence of hypertension in India was 30.7% and the prevalence among women was 23.7%.[5]

Changes in lipids and lipoproteins at the time of menopause may contribute significantly to the increased risk for the development of CVD over the lifetime of women. Research has documented that serum lipids and lipoproteins are altered as a consequence of menopause, resulting in a more atherogenic lipid profile. During menopause, a woman's ovaries stop making eggs and they produce less estrogen and progesterone. The lower hormones may cause menopausal symptoms and long-term health effects such as osteoporosis, CVD, and psychiatric disease.[6]

Due to increased longevity and awareness, most women seek help of the clinicians for the management of these diseases. Soybean and its products are rich in isoflavone compared with the other plants. They are referred as phytoestrogens by binding to estrogen receptor and affecting estrogen mediated process.[7] In the past few years, there has been increasing interest in the potential role of phytoestrogens in the prevention of CVD.[8,9] Phytoestrogens mainly consist of isoflavone, lignans, and coumestans. Soy isoflavone is heterocyclic phenols that have similar structure to 17 β estradiol and selective estrogen receptor modulator and its important constituents are genistein, daidzein, and glycitein.[10] Isoflavone exerts its effect through estrogen receptor and promotes its natural effect.

Accordingly, the purpose of this study was to evaluate the beneficial effect of soy isoflavones in the form of soyflour on BP and serum lipid of Rajasthani postmenopausal women.

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Materials and Methods

Selection of Subjects

A preliminary assessment on 322 women aged between 45 and 55 years was conducted in Udaipur city, Rajasthan, India for the screening of subjects for intervention trial. CVD risk assessment tool was used for the identification of women with low, medium, high, and very high risk of CVD.[11] Exclusion criteria were: Currently or previously taking any estrogen therapy, soy products or supplements, regular use of medication (e.g., lipid lowering drugs, antidiabetic medications, and antihypertensive drugs), hyper or hypothyroidism, kidney, liver, infectious diseases, breast cancer or any cancer, and allergic reaction to soy consumption. Finally, a total of 60 postmenopausal women who were at medium risk of CVD, who met the inclusion criteria, and willingness to participate were enrolled in the study [Figure 1]. The study design was approved by the Research Committee of the University. A written informed consent was obtained from each participants and they participated in the study on a voluntary basis.

Method

This was a 16 weeks randomized and placebo controlled trial with a follow-up examination at the end of the study. Participants were assigned randomly to either treatment or control group. The treatment group received daily a sachet of 40 g soyflour containing 52.62 mg isoflavones. The control group was encouraged not to change their usual dietary habits and lifestyles and was instructed to avoid taking soybean and soybean products. The participants were visited every week. The treatment group was provided with seven packages of 40 g of soyflour for 1 week supply. Refills were provided the following week. They were trained on how they could prepare their chapatti (Indian bread) with soyflour. The nutrient composition of soyflour is shown in Table 1.

Outcome Measures

All assessments were done at baseline and after completion of intervention.

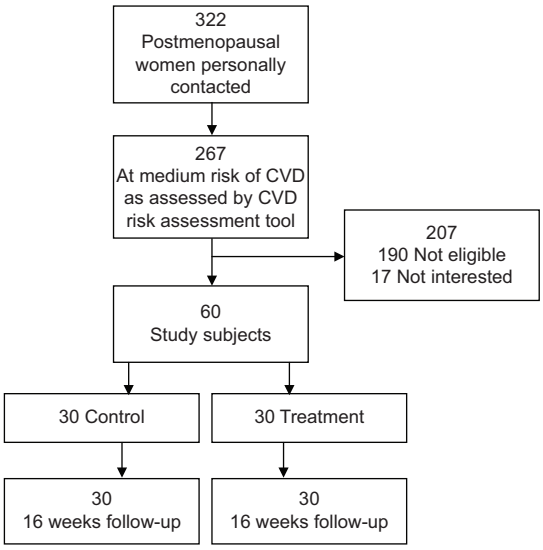

Figure 1: Participant flow chart

Nutritional assessment

Assessment of nutrient intake was based on 3-day dietary record. The 3-day food record was analyzed using computer program developed by Kaur.[12] During the survey, anthropometric measurements were measured for height and weight. To obtain the body mass index (BMI), weight in kg was divided by square of height in meter square.

Biophysical assessment

BP of the participants was assessed twice at the right arm after 10 min sitting using calibrated mercury sphygmomanometer. The average of three seated systolic and diastolic BP measurements were used for data analysis.

Biochemical assessment

After 10–12 h overnight fasting, 10 ml of venous blood was drawn and was collected into vials. Serum was separated by centrifugation within 15 min of collection. All blood samples were analyzed in the biochemical laboratory. Serum total cholesterol (TC), serum triglyceride (TG), and high density lipoprotein-cholesterol (HDL-c) were estimated by enzymatic methods using estimation kits on fully auto analyzer SELECTRA E (Merck Company). The levels of low density lipoprotein-cholesterol (LDL-c) were calculated by Friedwald formula (TC – HDL-c – 0.20 × TG). Very LDL-c (VLDL-c) levels were calculated by formula (TG/5).

Statistical Analysis

All data were analyzed using SPSS for Windows (Version 15) to obtain descriptive and inferential statistics. Independent t-test was used to compare the means of variables before and after intervention. Paired *t*-test was used to compare means of BP and lipid profiles before and after intervention. The percentage change for each variable was calculated by the formula [(E - B)/B] × 100, while E is the value after intervention and B is the baseline value. Values of $P < 0.05$ were considered significant.

Results and Discussion

Demographic Profile and Diet

All participants completed the entire study. The demographic characteristics of the subjects in treatment group and control group are shown in Table 2. There were no significant differences within the groups in the selected variables (age, height, weight, BMI, and age at menopause) at baseline. The mean macronutrient intake of the treatment and placebo group is shown in Table 3.

Table 1: Nutrient content of soyflour on dry weight basis (per 100 g)

Nutrients	*Mean*
Protein (g)	44.07
Fat (g)	19.14
Ash (g)	4.70
Crude fiber (g)	5.25
Carbohydrate (g)	26.82
Energy (kcal)	455.89
Calcium (mg)	198
Isoflavone* (mg)	131.55

*Fresh weight basis

No significant differences were observed between the groups at baseline point. Intake of calorie, protein, fat, and fiber was found to be significantly increased in the treatment group at the end of the study but within the recommended daily allowances.

Effect of Soyflour Supplementation on BP

Systolic BP (SBP) and diastolic BP (DBP) are shown in Table 4. No significant difference in the baseline values of these variables was observed. After 16 weeks of intervention, mean of SBP and DBP of the treatment group was significantly lower ($P < 0.05$) from baseline values. Decrease in percentage change observed after intervention was 6.28% in SBP and 4.73% in DBP. Control group did not show any significant change in above parameters.

In the present study, positive effects of the intervention were observed in the reduction of BP of the experimental subjects. Isoflavones, the suspected active ingredients in soy, were directly evaluated in a recent meta-analysis of 14 randomized controlled trials with a total of 789 non-hypertensive participants ingesting 25–375 mg of soy isoflavones for 2–24 weeks where SBP decreased, on average, by 1.9 mm Hg.[13] Meta-analysis by Liu *et al.* showed a mean decrease of 2.5 mm Hg for SBP and 1.5 mm Hg for DBP in the soy isoflavones-treated group compared to placebo.[14]

Table 2: Demographic characteristics of the subjects by the treatment group[#]

Characteristic	*Control (n=30)*	*Treatment (n=30)*
Age (y)	54.53±0.85	54.27±1.06
Height (cm)	151.97±4.87	150.90±6.66
Weight (kg)		
Week 0	49.16±0.97	48.82±1.48
Week 16	49.56±1.60	50.36±1.67
BMI (kg/m^2)		
Week 0	21.39±1.35	21.58±1.65
Week 16	21.53±1.15	22.27±1.65
Age at menopause (y)	47.12±2.90	47.11±2.97

[#]Arithmetic $\bar{x}$±SEM. There were no significant differences between the treatment groups in age, height, or age at menopause (ANOVA).
ANOVA: Analysis of variance, BMI: Body mass index

Subgroup analysis of hypertensive subjects revealed that a greater BP reduction was identified in the soy isoflavone-treated group compared to placebo. As compared to this, findings of the present study related to percent change was found somewhat higher in both SBP and DBP.

High BP raises the hazard of vascular damage by favoring inflammatory processes, thus increasing the risk of CVD. Supplementing menopausal women, with isoflavones, enhanced lumen dilation of vessels.[15] Constituents other than isoflavones have revealed to own BP lowering qualities. BP lowering effect of isoflavones by communicating with estrogen-response component of gene raise the endothelial nitric oxide which boost up arterial blood flow.[16] The consequences of isoflavones on endothelial depend on persons potential to convert daidzein into equol.[8]

Effect of Soyflour Supplementation on Lipid Profile

Table 5 presents data pertaining to the values of different fractions of lipid profile before and after the intervention study. No significant difference was found between control and experimental group during the initiation of the study regarding TC, TG, LDL-c, HDL-c, and VLDL-c parameters of lipid profile. Thus, there was no biasness in the selection of control and experimental samples.

The intervention resulted in a reduced level of TC, TG, LDL-c, and VLDL-c from 234.97 ± 21.00 mg/dl to 194.34 ± 16.97 mg/dl, 176.67 ± 46.12 mg/dl to 137.4 ± 27.16 mg/dl, 157.16 ± 21.52 mg/dl to 118.61 ± 18.85 mg/dl, and 35.33 ± 9.22 mg/dl to 27.48 ± 5.43 mg/dl, respectively. There was a significant decrease ($P < 0.05$) in the mean values of TC, TG, LDL-c, and VLDL-c. The intervention resulted in an increased level of HDL-c from 42.48 ± 7.24 mg/dl to 48.24 ± 7.43 mg/dl which was significant ($P < 0.05$).

Soyflour intervention had a definite positive effect on the cholesterol levels of the experimental group. Results of the present study are in tune with the findings of Jassi *et al*.[17] They found a significant improvement in serum TG in postmenopausal women consuming 60 mg isoflavones daily for 12 weeks. Furthermore, Bakhtiary *et al.* reported that soy nut significantly improved LDL-c

Table 3: Macronutrient intakes at baseline (week 0) and at the endpoint (week 16) by the treatment group[#]

Macronutrient	*Placebo (n=30)*			*Treatment (n=30)*		
	Week 0	*Week 16*	*t-value*	*Week 0*	*Week 16*	*t-value*
Energy (kcal)	1471.10±112.50	1493.0±102.85	0.311^{NS}	1428.80±118.44	1602.70±101.24	0.000*
Carbohydrate (g)	203.50±11.53	206.46±15.55	0.363^{NS}	198.14±18.74	205.98±24.16	0.175^{NS}
Protein (g)	43.98±3.95	45.52±2.71	0.027*	43.29±3.83	54.83±4.07	0.000*
Fat (g)	50.10±7.09	50.51±6.56	0.769^{NS}	48.82±5.20	57.62±3.54	0.000*
Fibre (g)	14.01±3.15	13.96±2.66	0.949^{NS}	13.13±3.31	21.54±2.76	0.000*

[#]Arithmetic $\bar{x}$±SEM. Values are based on data from 3-day food records. There were no significant effects of time or group and no significant group×time interaction (two-factor ANOVA). ANOVA: Analysis of variance

Table 4: Mean (SD) values of blood pressure at baseline (week 0) and after intervention (week 16)

Parameters	*Groups*	*Baseline*	*After intervention*	*p*$^{\delta}$	*Percent change*
		Mean±SD	*Mean±SD*		
SBP (mmHg)	Control	138.40±14.79	137.67±11.28	0.526^{NS}	0.52↓
	Treatment	140.60±10.86	131.77±9.97	0.000*	6.28↓
	P$^{\xi}$	0.514NS	0.036*		
DBP (mmHg)	Control	88.07±9.75	88.20±8.58	0.775^{NS}	0.14↑
	Treatment	90.77±9.55	86.47±7.45	0.000*	4.73↓
	P$^{\xi}$	0.283NS	0.407NS		

SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, δ: *P*-value as calculated by *t*-test, ξ: *P*-value as calculated by independent sample *t*-test, * Significant at 5% level, NS: Non significant, ↑indicates increase, ↓indicates decrease

Table 5: Mean (SD) values of lipid profile at baseline (week 0) and after intervention (week 16)

Parameters	*Groups*	*Baseline*	*After intervention*	p^{δ}	*Percent change*
		Mean±SD	*Mean±SD*		
TC (mg/dl)	Control	229.25±20.03	230.81±17.82	0.412^{NS}	0.68↑
	Treatment	234.97±21.00	194.34±16.97	0.000*	17.29↓
	P^{ξ}	0.285^{NS}	0.000*		
TG (mg/dl)	Control	172.70±39.41	168.70±36.52	0.051^{NS}	2.31↓
	Treatment	176.67±46.12	137.40±27.16	0.000*	22.22↓
	P^{ξ}	0.722^{NS}	0.000*		
HDL-c (mg/dl)	Control	44.39±10.90	45.78±9.73	0.054^{NS}	3.13↑
	Treatment	42.48±7.24	48.24±7.43	0.006*	13.55↑
	P^{ξ}	0.427^{NS}	0.276^{NS}		
LDL-c (mg/dl)	Control	150.32±19.47	151.29±18.19	0.615^{NS}	0.64↑
	Treatment	157.17±21.52	118.61±18.85	0.000*	24.53↓
	P^{ξ}	0.201^{NS}	0.000*		
VLDL-c (mg/dl)	Control	33.27±9.94	33.74±7.30	0.734^{NS}	1.41↑
	Treatment	35.33±9.22	27.48±5.43	0.000*	22.21↓
	P^{ξ}	0.408^{NS}	0.000*		

SD: Standard deviation, TC: Total cholesterol, TG: Triglyceride, HDL-c: High Density Lipoprotein, LDL-c: Low Density Lipoprotein, VLDL-c: Very Low Density Lipoprotein, δ: *P*-value as calculated by *t*-test, ξ: *P*-value as calculated by independent sample *t*-test, *Significant at 5% level, NS: Non significant, ↑indicates increase, ↓indicates decrease

and VLDL-c ($P < 0.05$). Serum TC decreased significantly in the soy nuts group as compared with the control group ($P < 0.005$).[18] In another study, Bhuiyan *et al*. showed that daily consumption of soymilk containing ˷30 mg isoflavones for 52 days significantly improved TG ($P = 0.001$) and HDL-c ($P = 0.032$) in Bangladeshi postmenopausal women.[19]

In the present study, estrogenic activity of soy isoflavone was recognized on lipid profile. There are several possible mechanisms for the lipid-lowering effects of isoflavone containing soy protein. The structural similarity between soy isoflavones and estradiol suggests that isoflavones may elicit estrogenic effects. It also has been proposed that isoflavones in soy may act as a selective estrogen receptor modulator and exert an effect on lipid metabolism through their biological similarities to estrogens.[20]

Conclusion

The results of this study showed that soy inclusion as part of the daily diet has a beneficial effect on BP in postmenopausal women having medium risk of CVD. A significant improvement in atherogenic lipids was also found. This study was performed in the free-living state; therefore, dietary soy may be a practical, safe, and inexpensive modality to reduce TC, TG, LDL-c, VLDL-c, SBP, DBP, and increase in HDL-c. Using soy foods to replace foods, high in animal protein that contains fat and cholesterol may help improve atherogenic lipid profiles and BP and confer benefits to cardiovascular health in postmenopausal women.

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