



Research article

Textured soybean protein improved level of glycated albumin, LDL-Cholesterol, and protein intake in prediabetes postmenopausal overweight women

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Abstract: *Background:* Indonesia has been increasing in health issues such as obesity, diabetes mellitus (DM), cardiovascular diseases (CVD), stroke and others. Healthy lifestyle of improving dietary habit with food consumption is considered effective to prevent these health issues. Soybean-based food is considered as food-alternative for plant-based protein and its ability to push down global warming rate. *Objective:* This study aims to test the effect of Textured Soybean Protein (TSP) on level of Glycated Albumin (GA) and lipid profiles in prediabetes overweight postmenopausal women. *Methods:* A parallel study design consisted of two groups: intervention group provided with TSP contains 30 grams protein and control group, with study duration of 21 days. Each group consists of 26 postmenopausal women with criteria of overweight with fasting blood sugar level of 120–200 mg/dL (prediabetes). The data was analyzed by unpaired and paired t-test. *Results:* TSP has significant influence on the change of GA level (3.4% reduction, $p < 0.05$) and LDL Cholesterol (LDL-C) (6.0% reduction, $p < 0.05$). TSP also improve the protein consumption of 18.1%. *Conclusions:* The provision of TSP for 21 days could improve GA and LDL-C significantly. In longer term, TSP is expected to improve of lipid profiles, insulin resistance and controlling weight and BMI.

Keywords: soybean proteins; prediabetes; postmenopausal; overweight; protein intake; macronutrient intakes; glycated albumin; lipid profile; LDL Cholesterol; sustainability

1. Introduction

The increase in overweight and obesity prevalence across the world is generally accompanied by diseases such as diabetes mellitus (DM), cardiovascular diseases (CVD), stroke, hypertension, and other metabolic syndromes. In Indonesia, based on the national basic health research (Riskesdas), the prevalence of overweight (BMI 25–27 kg/m²) was increased from 8.6% to 13.6%, while obesity (BMI > 27 kg/m²) increased from 10.5% to 21.8% [1]. Then, more than half of the total deaths in Indonesia are due to non-communicable diseases, where the top three are stroke, CVD, and DM [2].

The International Diabetes Federation (IDF) data mentioned in 2017 that the number of DM patients reached 425 million patients in the world, there are 10 million people as DM patients in Indonesia, making in the 6th largest number of patients in the world [3]. DM patients in Indonesia increase from 6.9% to 8.5% between 2013 and 2018 [1]. DM cases generally begin with an increase in weight, and obesity often occurs in parallel with worsening lipid profiles. The impact of such diseases resulted in increase in health costs and reduction in quality of life of patients. Improving the nutrition-related health conditions are considered to be the most effective through lifestyle changes and a way to improve food consumption.

Soybean is an intensely studied plant-based protein source for its role in improving health status. Meta-analysis results show that soy protein consumption affects positively the lipid profile, particularly in the case of adults without diabetes [4,5]. Isoflavone and other soybean-related proteins has a role in reducing plasma glucose [6,7] and improving insulin resistance levels [7,8]. There are several tests to diagnose diabetes mellitus. Fasting blood glucose test is used to show glucose level condition in short period and HbA1c analysis to show glucose level condition for the last 2–3 months period. Glycated Albumin (GA), the process of non-enzymatic albumin glycation in two weeks turn-over rate which depends on glycemia and protein in bloodstream, also be used as biomarker for glycemic status and have shorter turn-over period compared with HbA1c [9]. The similar high accuracy of HbA1c and GA makes GA is efficiently more applicable for intervention [9]. Taken into consideration that currently there is no research conducted on TSP consumption towards GA, this research might be the first to examine the TSP effect in improving prediabetes subjects with GA and lipid profiles as biomarkers.

2. Materials and methods

2.1. Study design overview and ethical approval

The study design was a quasi-experimental research design, with control group pretest-posttest. There were 2 groups: additional TSP in usual daily meal as intervention group (TSP Group) and the usual daily meal as control group (N-TSP Group). The study protocol was approved by the Ethics Committee of the Faculty of Medicine Universitas Indonesia (Protocol number 17-09-0895) and has been performed properly in accordance with the Declaration of Helsinki World Medical Association. Informed consent was obtained from all participants started from the beginning of early screening process.

2.2. Participant recruitment and eligibility

Sample number was calculated using Comparing Two Population Means formula ($n = 24$), formula for a continuous output and equal sample sizes in both groups to comparing two means [49]. There are nine Integrated Health Center located in Depok, a peri-urban area located in southern Jakarta, Indonesia. The early screening process was performed by conducting screening based on the inclusion criteria. The inclusion criteria were age range 45–60 years, housewife with normal activity, prediabetes measurement with peripheral fasting blood glucose test (120–200 mg/dL), menopause for at least 1 year, and BMI 25–30 kg/m². The exclusion criteria were having chronic diseases such as diabetes mellitus, hypertension, cardiovascular diseases, stroke, hyperthyroidism, and others.

On the first screening process, the potential subjects were explained about the study and asked their participation in peripheral blood glucose screening. If the peripheral blood glucose level of the potential subjects was within the range for prediabetes, they would be offered for further participation in this study. Thus, these subjects were measured for their anthropometry data and interviewed basic information. Since the intervention material was food, area randomization for grouping was conducted. TSP Group resided in the area/place quite distant from the N-TSP group to avoid the acknowledgment of each treatment. The biomarker data collected at baseline and endline were blood withdrawn for GA and lipid profiles: Total Cholesterol (TC), LDL Cholesterol (LDL-C), HDL Cholesterol (HDL-C), and Triglyceride (TG). Analysis was performed in an international standardized laboratory. The basic analysis for GA is using enzymatic methods. First, the amino acid of glycated endogen and peroxide is eliminated with ketoamine oxide and peroxide. GA is hydrolyzed into amino acid or peptide by specified albumin proteinase. Then, glycated amino acid or peptide is deoxidated by ketoamine oxide. This will form hydrogen peroxide which can be measured quantitatively. Albumin level is measured with bromocresol purple method and GA level is calculated as GA percentage on total albumin.

2.3. Dietary intervention

Various shapes of TSP (Fuji Oil Co. Ltd) are shown in Figure 1. One portion of 50 grams dry matter TSP contains 30 grams protein, was processed to various menu served in daily meal box. The processed menu was varied every single day to avoid boredom. Cooking process involved soaking dry matter TSP in boiled water for 3–5 minutes, strained and drained the water out, then sautéed with spices [10]. After sautéed, TSP was cooled off at room temperature before being placed in the meal box then home delivered every single day of treatment to each subject in TSP Group. In the following day, the subjects were asked about TSP consumption on the previous day, if any remains, the TSP left over would be weighed. Both groups were asked to maintain their daily activities. Nutrition surveys with 3 days 24-hour recall methods were conducted on Baseline and Endline.



Figure 1. Various shapes of TSP.

2.4. Statistical analysis

Descriptive analysis was performed for every variable in both groups of treatment, including mean \pm SD, n and percentage (%), % delta (Baseline-Endline)/Baseline). Mean and standard deviation were analyzed for protein consumption as well as blood biomarker i.e., GA, TC, LDL-C, HDL-C and TG. Statistical tests were performed to determine the intervention effect, which compares baseline and endline within the group using a paired t-test and the unpaired t-test was conducted to compare between treatment groups.

3. Results

3.1. Characteristic of the subjects

During the pre-screening process, 107 potential subjects met the inclusion criteria. Three women refused for further participation in the research, hence 104 subjects continued the screening process. Next, there were 46 women excluded from the research, whose fasting blood glucose level of 36 women had < 120 mg/dL (normal) and 10 women had > 200 mg/dL (DM, referred to health facility). Fifty-eight women became the subjects, 32 subjects in TSP Group and 26 subjects in N-TSP Group. Twenty-six subjects remained in TSP Group (incomplete data: 1 subject left out the town, 4 subjects didn't consume TSP throughout research period, and 1 subject refused blood withdrawn), while in N-TSP Group remained the same number until the end of research period.

Table 1 shows the subjects' characteristics. Most of the subjects were older than 50 years in both the N-TSP group (88.5%) and TSP (80.5%), housewives (92.3% and 88.5%, respectively), while BMI status of overweight (61.5% and 50%, respectively) and obese (38.5% and 50%, respectively) showed even distribution. The occupation characteristics of the participants in this study are similar to those of the peri-urban population in Indonesia.

Table 1. Subject's characteristic of N-TSP and TSP group.

Variables	N-TSP		TSP	
Occupation				
House wife	24	92.3	23	88.5
Working at home	2	7.7	3	11.5
Age (45–60 years old)				
Mean \pm SD	55.6 \pm 3		55.4 \pm 5	
	n	%	n	%
< 50 years old	3	11.5	5	19.2
\geq 50 years old	23	88.5	21	80.8
BMI Status (kg/m ²)				
mean \pm SD	57 \pm 6.5		62 \pm 12.0	
	n	%	n	%
Overweight (25–27)	16	61.5	13	50
Obese (>27)	10	38.5	13	50

3.2. Consumption of TSP dishes

There were 10 TSP dishes provided to the TSP Group and changed daily to avoid boredom [10]. The subjects of the TSP group were provided with 50 grams/day (g/day) dry matter of TSP, equivalent to 30 grams protein. On average, they consumed 45.8 g/day (92%) of the food materials. Dry matter of 4.2 g/day (8%) remained due to the feeling full (62%), dislike the flavor (25%), and lost appetite due to feeling sick (13%) (Figure 2).

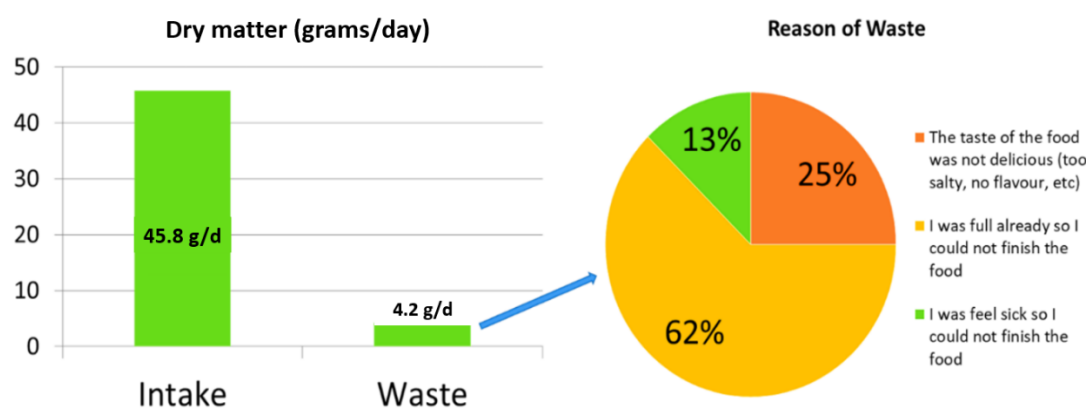


Figure 2. Average TSP consumption and remains.

Table 2 shows energy and macronutrient intakes of both groups. The protein consumption before the intervention was not different between the TSP and N-TSP groups. The baseline protein consumption of the N-TSP group was 54.0 ± 18.3 (94.7% Recommended Dietary Intake or RDA) and the TSP group was 49.4 ± 13.0 (87.0% RDA), meaning that the baseline consumption in both groups was similar. After 21 days of intervention, we could observe a significant increase in protein consumption of 18.1% ($p < 0.05$) in the TSP group, while the protein consumption did not significantly change the N-TSP group. TSP groups had significant decrease of lipid intakes. The quality of soy protein is found higher than other plant protein and similar to animal protein [11]. It is measured by Protein Digestibility Corrected Amino Acid Score (PDCAAS) and Digestible Indispensable Amino Acid Score (DIAAS) [11,12]. The soy protein DIAAS score is about 0.9, above the minimum score for high-quality protein category (FAO, score 0.75). Its components are able to improve the cells' signal line for energy homeostatis and to arrange inflammation parameters related to diabetes pathophysiology [13]. Arginine has strong antioxidant and hypocholesterolemia effects [14]. In this study, the protein intake in TSP group has increased 18.1%, similar results with the findings at previous study soy-protein could increase 50% of RDA [15].

Soybean is low in carbohydrate, which is beneficial for people risk in diabetes [16]. In this study, carbohydrate intake has decreased 7.5% in TSP group, while N-TSP groups has increased 6.3%. The main lipid composition in soybeans is polyunsaturated fatty acids (PUFA) which have lipid improvement profile, about 46%–62% consisted of linoleic acid and linolenic acid [17]. Isoflavone in soybeans helps to control cholesterol, LDL-C, triacylglycerol, and improve HDL-C, depends on its provision amount and intervention duration [5]. In this study, TSP groups has decreased lipid intake of 39.3%. TSP might be able to replace unhealthy snacks during our study, such as less intake of high

lipid foods that commonly found in fried foods. The intake of lipid and carbohydrate in TSP groups has direct effect on their energy intake decrease compared to N-TSP group (16.7% vs 2.4%). In overweight individuals, the decrease of energy intake is expected to improve BMI level which eventually lower the risk of diabetes mellitus and other degenerative diseases.

Table 2. Energy and macronutrients intakes in both N-TSP and TSP group.

Energy and Nutrient Intake	N-TSP (n = 26)	TSP (n = 26)	p value**
Energy (g/day)			
Baseline	1931 ± 162	1984 ± 189	NS
Final	1884 ± 162	1653 ± 197	S
% delta	↓2.4	↓16.7	S
p value*	NS	S	
Protein (g/day)			
Baseline	54.0 ± 18.3	49.4 ± 13.0	NS
Final	49.6 ± 14.0	58.6 ± 11.3	S
% delta	↓8.1	↑18.1	S
p value*	S	S	
Lipid (g/day)			
Baseline	88.8 ± 18.6	89.8 ± 17.4	NS
Final	80.6 ± 13	54.5 ± 14.7	S
% delta	↓9.2	↓39.3	S
p value*	S	S	
Carbohydrate (g/day)			
Baseline	240 ± 48	262 ± 35.4	NS
Final	255 ± 33.3	242 ± 43.4	NS
% delta	↑6.3	↓7.5	NS
p value*	NS	NS	

Note: Significant differences (p value < 0.05); * = within group; ** = between groups; % delta = (Baseline-Endline)/Baseline; S denotes significant (p value < 0.05); NS denotes not significant (p value > 0.05).

3.3. Profiles of blood biomarkers

Table 3 shows the change in blood biomarkers within groups (baseline and endline) and between groups (N-TSP and TSP). After 21 days of treatment, the GA level in the TSP and N-TSP group was reduced, but the statistically significant reduction only occurred in the TSP group, 3.4% (p < 0.05), while in the N-TSP group, it was reduced by 1.5% (p > 0.05). In the TSP group, there was a significant reduction in LDL-C, 8.6 mg/dL or 6% (p < 0.05). For TC and TG indicators, even though there was reduction of 7.2 mg/dL (3.1%) and 18.0 mg/dL (11.8%) but there was no significance found in this reduction. HDL-C shows no improvement, instead, reduced slightly of 2 mg/dL (3.8%). Concerning the N-TSP group, the changes in the TC, LDL-C, HDL-C, and TG was found not significant. In summary, we could conclude from these results that the improvement in all blood biomarker indicators were relatively better in the TSP group compared with the N-TSP group, in which particularly significant on GA and LDL-C level (Figure 3).

Table 3. Biomarker profiles changes at Baseline and Endline.

Biomarker Profiles	N-TSP (n = 26)	TSP (n = 26)	p value**
	Mean ± SD	Mean ± SD	
Glycated albumin (%)			
Baseline	13.7 ± 2.0	14.7 ± 2.8	NS
Endline	13.5 ± 2.1	14.2 ± 2.4	NS
% delta	↓1.5	↓3.4	S
p value*	NS	S	
TC (mg/dL)			
Baseline	235.5 ± 40.3	235.1 ± 43.9	NS
Endline	226.5 ± 49.8	227.9 ± 39.1	NS
% delta	↓3.8	↓3.1	NS
p value*	NS	NS	
LDL-C (mg/dL)			
Baseline	135.2 ± 37.9	144.0 ± 36.4	NS
Endline	135.3 ± 38.2	135.4 ± 32.9	NS
% delta	↑0.1	↓6.0	S
p value*	NS	S	
HDL-C (mg/dL)			
Baseline	50.7 ± 7.8	52.2 ± 11.8	NS
Endline	49.5 ± 6.9	50.2 ± 8.9	NS
% delta	↓2.4	↓3.8	NS
p value*	NS	NS	
Triglycerida			
Baseline	161.3 ± 89.6	152.6 ± 88.3	NS
Endline	143.6 ± 77.6	134.6 ± 82.6	S
% delta	↓10.9	↓11.8	NS
p value*	NS	NS	

Note: Significant differences (p value < 0.05); * = within group; ** = between groups; % delta = (Baseline-Endline)/Baseline; S denotes significant (p value < 0.05); NS denotes not significant (p value > 0.05).

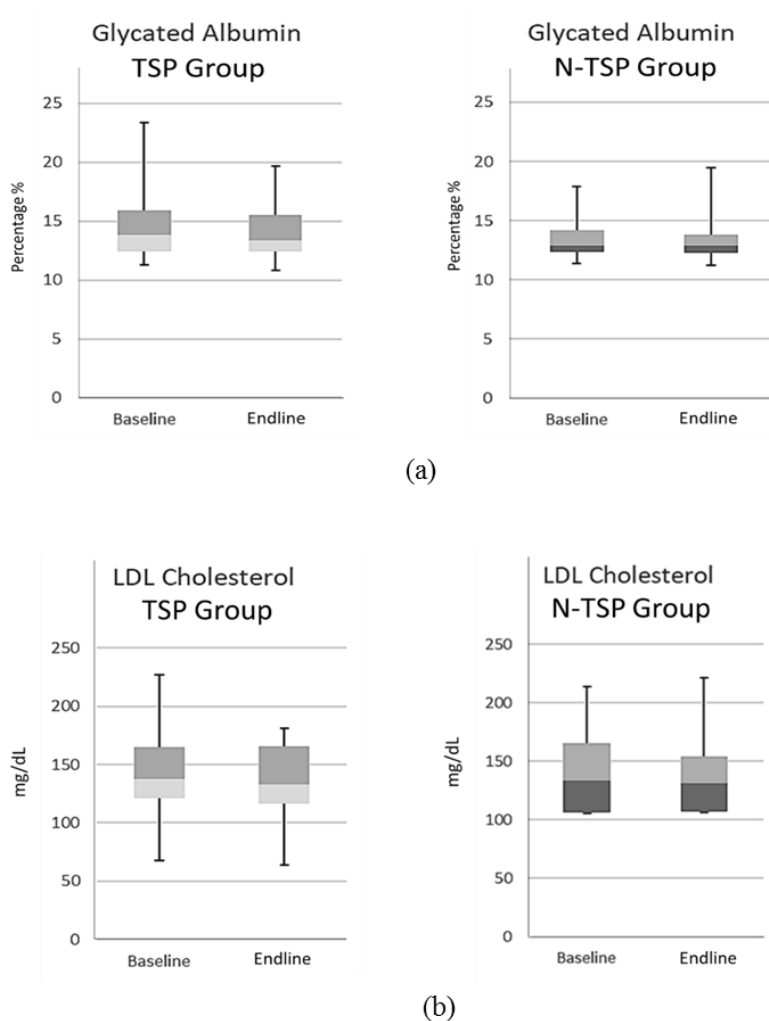


Figure 3. Representation of Glycated Albumin (a) and LDL Cholesterol (b) profiles at Baseline and Endline of 21 days 50 grams dry matter/days of TSP consumption.

4. Discussion

Textured soybean protein that was provided to TSP group is a low-fat protein source which contains amino acid [18]. A relatively low content but non-restrictive amino acid is methionine which also available in both soybean and rice, which act as staple food for Indonesian. Hence, the mixed rice and soybean can provide full amino acids which are equivalent with animal source foods. TSP is proper food, especially for menopausal women, who are at risk of DM and hypercholesterolemia. The content of 30 grams protein in 50 grams TSP is equivalent to 47% RDA. In the TSP group, the protein intake of subjects increased by 18.1% at the endline, compared with the baseline. Hence, the subject could reach 100% RDA. In Indonesia, the plant-based protein consumption mainly come from Tempe. Tempe doesn't have meaty texture attributes like TSP, makes TSP has a potential as food alternative as meat substitution rather than Tempe.

Overall, energy and macronutrients intakes were significantly changed in TSP group compared to N-TSP group. The intake of lipid and carbohydrate in TSP groups has contributed to energy intake decrease much higher than N-TSP group, while protein intake of TSP group has increased much higher

compared to N-TSP. TSP has favorable effects to dietary changes and resulted in biomarker profiles improvement. Unhealthy diet of high lipid and carbohydrate intakes (fried foods) could be controlled with TSP with intervention duration of 21 days. It is expected that in longer duration of study, similar dietary changes can form favorable habits to maintain healthy life especially in people with high risk of degenerative diseases.

HbA1c is a widely used as DM biomarker. However, this biomarker could only indicate the conditions of the past 2–3 months, unsuitable for shorter period to see the effects of an intervention. GA is the product of the non-enzymatic albumin glycation process. The GA rate depends on glycemia and blood protein levels and thus could be used as a glycemic status biomarker. Since albumin has a short half-life (3 weeks), GA could be used as an early response to an intervention [9]. GA is the higher glycated part of fructosamine measured by a standardized enzymatic methodology, easy and fast to perform. Similar to HbA1c, the GA level is relatively unaffected by other metabolic systems. In several cases, GA is better in monitoring several diabetes mellitus patient cases [19] and could control the dosage and medication change if required could provide faster response compared with HbA1c [20]. GA has accurate diagnostic and ideal to assess diabetic microvascular complications [21]. Furthermore, this is confirmed by two studies that showed that GA was able to predict microvascular complications and cardiovascular events in both DM patients and the general population [22,23]. Taken into consideration that we found no previous study on the effect of TSP for GA, this research might be the prior one in the literature which examine the effect of TSP in improving the condition of DM-risk patients within a short period using GA and lipid profile biomarkers.

In this study, the GA level reduced significantly after the provision of TSP for 21 days. The GA reduction is expected to reduce the formation of advanced glycation end-products (AGEs). This is consistent with the results of a study of DM patients treated for 4 weeks in hospital, showing that the formation of AGEs reduced drastically along with the GA level reduction [24]. The reduction of GA and AGE levels in DM patients improved pancreatic damage and insulin production. The GA improvement also implicates importantly in the prevention of CVD [25]. Moreover, a study reported that the reduction of pancreatic beta cell function is related to the duration of subjects having DM that is linked with the increase of GA and the ratio of GA/HbA1c, although it is unknown if only HbA1c examination is needed [26]. This is supported by another study that GA is more effective than HbA1c to assess the glycemic variability level and postprandial glucose levels [23,27] also in a short time GA could be used to determine whether a treatment will be continued or need to be replaced [28].

A previous meta-analysis suggested that the provision of soybean products does not significantly affect the fasting blood glucose level, insulin, and HbA1c [29]. However, in this study it was found that soy protein provision or TSP had effects on the GA levels. Few studies on Asian populations in a small number of samples have clinically evaluated the use of GA to monitor the treatment of hypoglycemia [19]. One study showed that DM patients without insulin treatment showed a glycemic improvement [30]. They suggested that GA is more sensitive bio-maker for detecting short-time glycemic change comparing HbA1c. After 14 days of treatment, GA was also a very strong predictor of the HbA1c level on the day 90. This means that after 2 weeks of treatment, GA could confirm the result of HbA1c that could be obtained after long treatment [30].

In this study, 30 grams of protein was administered, which is slightly higher compared with the FDA USA recommendation that recommends 25 grams soy protein per day to reduce cholesterol [31] but lower compared with China, which recommends a soy protein consumption of 50 grams daily [32]. The TSP provision itself lasted for 21 days. Therefore, not all lipid profiles reduced significantly.

Significant reduction only occurred in LDL-C, which was reduced by 6%, while a reduction in TC (3.1%) and TG (11.8%) were not statistically significant. A previous study showed that the adaptation on protein diet has duration of 2–5 weeks [33] while another study showed that the protein improvement could happen after 3–6 weeks [34]. A study with the same duration (3 weeks) yielded soy food containing 25 grams soy protein also showed similar results, where reduction of TC amounted to 3.4%, LDL-C reduced 8.0%, and TG reduced 8.0%, but HDL-C did not show any changes [35]. Another study that provided short-time (4 weeks) intervention for postmenopausal women with abdominal obesity showed that dietary soy protein could reduce the TC level by 4% and indicated that the LDL-C level was 9% lower compared with those observed following the mixed-protein diet [36]. Although there was no significant difference at the percentage change, TG profile is significantly different at the endline between N-TSP group and TSP group. This might be caused by a slightly higher baseline value in N-TSP group compared with TSP group. There might be plausible effects in their dietary habits which affect their TG level and have a quite similar decrease as TSP group, though delta% in two groups showed no significance.

While other study that gave 120 grams bread fortified with soybean flour for 6 weeks to women with type 2 diabetes mellitus (T2DM) showed a non-statistically different reduction of TG serum of 3.7 mg/dL and LDL-C of 11.2 mg/dL and increased of TC level [37]. A study of 25 grams soy protein provision in 8 weeks showed TG reduction by 22.9% [38]. While another study that gave whole soy to postmenopausal women for 6 months showed a reduction of TG 7.4%, reduction of TC 1.3%, reduction of LDL-C 4.1%, and no change of HDL-C [39]. The meta-analysis conducted by Anderson et al. on 38 clinical studies showed a relationship between soy protein consumption and lipid profile improvement, especially LDL-C, although there was almost no change in HDL-C [4].

Previous studies have shown that soy protein could reduce TC, TG, and LDL-C even with no statistical differences, but could not improve HDL-C even with a long duration of intervention. Epidemiological studies have shown that soybean products could reduce TC, LDL-C, and TG in durations of less than 12 weeks. Hence, soy products could be used for nutritional therapy for dyslipidemia in T2DM patients [29]. A study in animal showed that soy protein can reduce insulin/glucagon ratio as well as reduced LDL-C in serum and liver by arranging the excretion of the hepatic transcription factor sterol regulatory element binding protein [40]. A meta-analysis reported that the improving effect of HDL-C was observed when the consumption period of soybean protein was 12 weeks or longer [4].

In Asia, historically there are many kinds of soybean processed traditional foods. In addition, these traditional foods contain high protein and act as isoflavone source. Each gram of soy food is estimated equal with 3.5 grams isoflavones [41]. Isoflavones in soybean can arrange the lipid metabolism by activating peroxisome proliferator-activated receptors [42] and reduce the lipoprotein lipase activity [43]. The meta-analysis done by Yeung and Yu [44] in 21 clinical studies suggested that isoflavone could significantly reduce TC, LDL-C and TG. Other meta-analysis reviewed 23 clinically studies reported that isoflavone significantly reduced TC 3.8%, LDL-C 5.3% and TG 7.3% also increase HDL-C 3.0% [5].

Soybean has amino acid content which has effect of hypocholesterolemia. Arginine and glycine are amino acid which stored quite big amount in soybean, are known on having effect in hypercholesterolemia. Other amino acids which have effect on hypercholesterolemia are lysine and methionine, stored less amount in soybean [45]. The ratio of arginine/lysine are higher in soybean compared to animal source food. In fact, it can inhibit the lipogenesis process [46]. Soybeans contain

two types of protein i.e., globulin 11S (Glycinin) and 7S (β -conglycinin) that can stimulate LDL-C receptor and reduce blood cholesterol [47]. The protein 7S is reported to reduce the accumulation of cholesterol in aorta hence can prevent of cardiovascular diseases and help in suppressing hunger center, while the protein 11 S has role as antioxidant, which animal source protein doesn't have [48].

The Sustainable Development Goals (SDGs) are a collection of 17 global goals designed to be a “blueprint to achieve a better and more sustainable future for all”. The SDGs, set in 2015 by the United Nations General Assembly and intended to be achieved by the year 2030, are part of UN Resolution 70/1, the 2030 Agenda. The effort to achieve the goals by food products is the more effective use of plant-based food ingredients. As a protein source, plant protein has higher production efficiency than animal protein. For this reason, the use of plant protein in particular soybean is expected to contribute not only to human health, but also for global sustainability.

5. Conclusions

In conclusion, the provision 50 grams dry matter TSP containing of 30 grams protein, for 21 days could improve the protein intake of the subjects, reduced energy, lipid and carbohydrate intakes, reduced GA and LDL-C levels significantly, and reduce TC and TG levels non-significantly. TSP is predicted to have high potential improving GA and the lipid profiles both in prediabetes and DM patients during a long-term consumption as an alternative food. Moreover, it represents a food source with a high nutrient intake that could contribute to reducing animal food burden globally.

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Conflict of interest

The authors declare no conflict of interest.

References

1. Ministry of Health Republic of Indonesia Research and Development Board (2019) *National report of basic health research 2018*, Jakarta: Ministry of Health.

2. Ministry of Health Republic of Indonesia (2017) Penyakit jantung penyebab kematian tertinggi, kemenkes ingatkan cerdas (Indonesian). Available from: [http://sehatnegeriku.kemkes.go.id/baca/umum/20170801/2521890/penyakit-jantung-penyebab-kematian-tertinggi-kemenkes-ingatkan-cerdik-2/#:~:text=Penyakit%20Jantung%20Penyebab%20Kematian%20Tertinggi%2C%20Kemenkes%20Ingatkan%20CERDIK,-0&text=Survei%20Sample%20Registration%20System%20\(SRS,yakni%20sebesar%2012%2C9%25](http://sehatnegeriku.kemkes.go.id/baca/umum/20170801/2521890/penyakit-jantung-penyebab-kematian-tertinggi-kemenkes-ingatkan-cerdik-2/#:~:text=Penyakit%20Jantung%20Penyebab%20Kematian%20Tertinggi%2C%20Kemenkes%20Ingatkan%20CERDIK,-0&text=Survei%20Sample%20Registration%20System%20(SRS,yakni%20sebesar%2012%2C9%25).
3. International Diabetes Federation (2017) *IDF diabetes atlas-8th edition*, Brussels: International Diabetes Federation.
4. Anderson JW, Johnstone BM, Cook-Newell ME (1995) Meta-analysis of the effects of soy protein intake on serum lipids. *N Engl J Med* 333: 276–282. <https://doi.org/10.1056/NEJM199508033330502>
5. Zhan SY, Ho SC (2005) Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. *Am J Clin Nutr* 81: 397–408. <https://doi.org/10.1093/ajcn.81.2.397>
6. Sathyapalan T, Rigby AS, Bhasin S, et al. (2017) Effect of soy in men with type 2 diabetes mellitus and subclinical hypogonadism: A randomized controlled study. *J Clin Endocrinol Metab* 102: 425–433. <https://doi.org/10.1210/jc.2016-2875>
7. Sathyapalan T, Javed Z, Rigby AS, et al. (2017) Soy protein improves cardiovascular risk in subclinical hypothyroidism: A randomized double-blinded crossover study. *J Endocr Soc* 1: 423–430. <https://doi.org/10.1210/js.2016-1068>
8. Jayagopal V, Albertazzi P, Kilpatrick ES, et al. (2002) Beneficial effects of soy phytoestrogen intake in postmenopausal women with type 2 diabetes. *Diabetes Care* 25: 1709–1714. <https://doi.org/10.2337/diacare.25.10.1709>
9. Ciaccio M (2019) Introduction of glycated albumin in clinical practice. *J Lab Precis Med* 4: 28. <https://doi.org/10.21037/jlpm.2019.08.02>
10. Sari IK, Utari DM, Kohno M, et al. (2020) Acceptance of textured soybean protein in Indonesian dishes and its effects on energy in overweight women. *Asian J Diet* 4: 171–177.
11. Hughes GJ, Ryan DJ, Mukherjea R, et al. (2011) Protein digestibility-corrected amino acid scores (PDCAAS) for soy protein isolates and concentrate: Criteria for evaluation. *J Agric Food Chem* 59: 12707–12712. <https://doi.org/10.1021/jf203220v>
12. Rutherford SM, Fanning AC, Miller BJ, et al. (2015) Protein digestibility-corrected amino acid scores and digestible indispensable amino acid scores differentially describe protein quality in growing male rats. *J Nutr* 145: 372–379. <https://doi.org/10.3945/jn.114.195438>
13. Das D, Kabir MD, Sarkar S, et al. (2022) Antidiabetic potential of soy protein/peptide: A therapeutic insight. *Int J Biol Macromol* 194: 276–288. <https://doi.org/10.1016/j.ijbiomac.2021.11.131>
14. Hadi A, Arab A, Moradi S, et al. (2019) The effect of l-arginine supplementation on lipid profile: a systematic review and meta-analysis of randomised controlled trials. *Br J Nutr* 122: 1021–1032. <https://doi.org/10.1017/S0007114519001855>
15. Utari DM, Rimbawan, Riyadi H, et al. (2011) Efek intervensi tempe terhadap profil lipid, superoksida dismutase, LDL teroksidasi dan malondialdehyde pada wanita menopause. Available from: <https://repository.ipb.ac.id/handle/123456789/51547>.
16. Feinman RD, Pogozelski WK, Astrup A, et al. (2015) Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition* 31: 1–13. <https://doi.org/10.1016/j.nut.2014.06.011>

17. Blasbalg TL, Hibbeln JR, Ramsden CE, et al. (2011) Changes in consumption of omega-3 and omega-6 fatty acids in the United States during the 20th century. *Am J Clin Nutr* 93: 950–962. <https://doi.org/10.3945/ajcn.110.006643>
18. World Health Organization (2007) Protein requirements of adults, including older people, and women during pregnancy and lactation, In: *Protein and amino acid requirements in human nutrition: Report of a joint WHO/FAO/UNU expert consultation (WHO technical report series 935)*, Geneva: WHO Press, 103–160.
19. Hsu P, Ai M, Kanda E, et al. (2015) A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan. *Atherosclerosis* 242: 327–333. <https://doi.org/10.1016/j.atherosclerosis.2015.07.037>
20. Danese E, Montagnana M, Nouvenne A, et al. (2015) Advantages and pitfalls of fructosamine and glycated albumin in the diagnosis and treatment of diabetes. *J Diabetes Sci Technol* 9: 169–176. <https://doi.org/10.1177%2F1932296814567227>
21. Freitas PAC, Ehlert LR, Camargo JL (2017) Glycated albumin: A potential biomarker in diabetes. *Arch Endocrinol Metab* 61: 296–304. <https://doi.org/10.1590/2359-3997000000272>
22. Selvin E, Rawlings AM, Grams M, et al. (2014) Prognostic utility of fructosamine and glycated albumin for incident diabetes and microvascular complications. *Lancet Diabetes Endocrinol* 2: 279–288. [https://doi.org/10.1016%2FS2213-8587\(13\)70199-2](https://doi.org/10.1016%2FS2213-8587(13)70199-2)
23. Selvin E, Rawlings AM, Lutsey PL, et al. (2015) Fructosamine and glycated albumin and the risk of cardiovascular outcomes and death. *Circulation* 132: 269–277. <https://doi.org/10.1161/CIRCULATIONAHA.115.015415>
24. Kisugi R, Kouzuma T, Yamamoto T, et al. (2007) Structural and glycation site changes of albumin in diabetic patient with very high glycated albumin. *Clin Chem Acta* 382: 59–64. <https://doi.org/10.1016/j.cca.2007.04.001>
25. Azadbakht L, Atabak S, Esmailzadeh A (2008) Soy protein intake, cardiorenal indices, and C-reactive protein in type 2 diabetes with nephropathy. *Diabetes Care* 31: 648–654. <http://doi.org/10.2337/dc07-2065>
26. Yoon HJ, Lee YH, Kim KJ, et al. (2015) Glycated albumin levels in patients with type 2 diabetes increase relative to HbA1c with time. *Biomed Res Int* 2015: 1–8. <https://doi.org/10.1155/2015/576306>
27. Koga M (2014) Glycated albumin; clinical usefulness. *Clin Chem Acta* 433: 96–104. <https://doi.org/10.1016/j.cca.2014.03.001>
28. Masumoto N, Otsuki H, Iwakawa S, et al. (2016) Usefulness of glycated albumin in decisions regarding the discontinuation of a diabetes drug and factors associated with poor glycemic control following discontinuation in patients with type 2 diabetes mellitus. *Diabetol Int* 8: 39–44. <https://doi.org/10.1007/s13340-016-0274-y>
29. Yang B, Chen Y, Xu TC, et al. (2011) Systematic review and meta-analysis of soy products consumption in patients with type 2 diabetes mellitus. *Asia Pac J Clin Nutr* 20: 593–602.
30. Lu JM, Ji LN, Li YF, et al. (2016) Glycated albumin is superior to glycosylated hemoglobin for glycemic control assessment at an early stage of diabetes treatment: A multicenter, prospective study. *J Diabetes Complications* 30: 1609–1613. <https://doi.org/10.1016/j.jdiacomp.2016.07.007>
31. Food and Drug Administration (1999) Food labeling: Health claims; soy protein and coronary heart disease. *Fed Regist* 64: 57700–57733.

32. Liu ZP, Li WX, Sun J, Liu C, et al. (2004) Intake of soy foods and soy isoflavones by rural adult women in China. *Asia Pac J Clin Nutr* 13: 204–209.
33. Ouellet V, Marois J, Weisnagel SJ, et al. (2007) Dietary cod protein improves insulin sensitivity in insulin resistant men and women: A randomized controlled trial. *Diabetes Care* 30: 2816–2821. <https://doi.org/10.2337/dc07-0273>
34. Harland JI, Haffner TA (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. <https://doi.org/10.1016/j.atherosclerosis.2008.04.006>
35. Padhi EM, Blewett HJ, Duncan AM, et al. (2015) Whole soy flour incorporated into a muffin and consumed at 2 doses of soy protein does not lower LDL cholesterol in a randomized, double-blind controlled trial of hypercholesterolemic adults. *J Nutr* 145: 2665–2674. <https://doi.org/10.3945%2Fjn.115.219873>
36. Nielen M, Feskens EJM, Rietman A, et al. (2014) Partly replacing meat protein with soy protein alters insulin resistance and blood lipids in postmenopausal women with abdominal obesity. *J Nutr* 144: 1423–1429. <https://doi.org/10.3945/jn.114.193706>
37. Moghaddam AS, Entezari MH, Iraj B, et al. (2014) The effects of consumption of bread fortified with soybean flour on metabolic profile in type 2 diabetic women: A cross-over randomized controlled clinical trial. *Int J Prev Med* 5: 1529–1536.
38. Acharjee S, Zhou JR, Elajami TK, et al. (2015) Effect of soy nuts and equol status on blood pressure, lipids and inflammation in postmenopausal women stratified by metabolic syndrome status. *Metabolism* 64: 236–243. <https://doi.org/10.1016/j.metabol.2014.09.005>
39. Liu ZM, Ho SC, Chen YM, et al. (2014) Whole soy, but not purified daidzein, had a favorable effect on improvement of cardiovascular risks: A 6-month randomized, double-blind, and placebo-controlled trial in equol-producing postmenopausal women. *Mol Nutr Food Res* 58: 709–717. <https://doi.org/10.1002/mnfr.201300499>
40. Mullen E, Brown RM, Osborne TF, et al. (2004) Soy isoflavones affect sterol regulatory element binding proteins (SREBPs) and SREBP-regulated genes in HepG2 cells. *J Nutr* 134: 2942–2947. <https://doi.org/10.1093/jn/134.11.2942>
41. Messina M, Nagata C, Wu AH (2006) Estimated Asian adult soy protein and isoflavone intakes. *Nutr Cancer* 55: 1–12.
42. Mezei O, Li Y, Mullen E, Ross-Viola JS, et al. (2006) Dietary isoflavone supplementation modulates lipid metabolism via PPARalpha-dependent and independent mechanisms. *Physiol Genomics* 26: 8–14. <https://doi.org/10.1152/physiolgenomics.00155.2005>
43. Orgaard A, Jensen L (2008) The effects of soy isoflavones on obesity. *Exp Biol Med* 233: 1066–1080. <https://doi.org/10.3181%2F0712-MR-347>
44. Yeung J, Yu T (2003) Effects of isoflavones (soy phyto-estrogens) on serum lipids: A meta-analysis of randomized controlled trials. *Nutr J* 2: 1–8. <https://doi.org/10.1186/1475-2891-2-15>
45. Matthan NR, Jalbert SM, Ausman LM, et al. (2007) Effect of soy protein from differently processed products on cardiovascular disease risk factors and vascular endothelial function in hypercholesterolemic subjects. *Am J Clin Nutr* 85: 960–966. <https://doi.org/10.1093/ajcn/85.4.960>
46. Potter SM (1995) Overview of proposed mechanism for hypocholesterolemic effect of soy. *J Nutr* 125: 606–614.

47. Duranti M, Lovati MR, Dani V, et al. (2004) The alpha' subunit from soybean 7S globulin lowers plasma lipids and upregulates liver beta-VLDL receptors in rats fed a hypercholesterolemic diet. *J Nutr* 134: 1334–1339. <https://doi.org/10.1093/jn/134.6.1334>
48. Torres N, Torre-Villalvazo I, Tovar AR (2006) Regulation of lipid metabolism by soy protein and its implication in diseases mediated by lipid disorders. *J Nutr Biochem* 17: 365–373. <https://doi.org/10.1016/j.jnutbio.2005.11.005>
49. Noordzij M, Tripepi G, Dekker F, et al. (2010) Sample size calculations: basic principles and common pitfalls. *Nephrol Dial Transplant* 25: 1388–1393. <https://doi.org/10.1093/ndt/gfp732>



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