Journal of Functional Food and Nutraceutical

CHOLESTEROL-LOWERING EFFECT OF SOY NUTS AND TEMPEH ON HYPERCHOLESTEROLEMIC SUBJECTS

Hermawati Nur Zulaikha[1]
Rendy Dijaya Muliadi[2]
Felicia Kartawidjajaputra[2*]
Lina Antono[2]

[1]Faculty of Health Medicine and Life Sciences, Health Food Innovation Management Department, Maastricht University campus Venlo, Nassaustraat 36, 5911 BV Venlo, Netherlands
[2]Health & Nutrition Science Department, Nutrifood Research Center, Jakarta, 13920, Indonesia

ABSTRACT

Exploration towards food with cholesterol-lowering property would be beneficial to reduce the incidents of cardiovascular caused by increasing number of people with hypercholesterolaemia. As much as 42 participants with total cholesterol (TC) levels ≥4.92 mmol/L were studied in a three-arms parallel intervention trial. As much as 72g soy nuts and 66g tempeh were consumed daily (25g soy protein/day) for six weeks, while control group was not given any sample. TC level and body composition were measured before and after the treatment for all groups. In soy nuts group, lower TC level was observed (-0.85±0.82 mmol/L, $p<0.05$) compared to the control group. Meanwhile in tempeh group, non-significant lower TC level was also observed (-0.40±1.19 mmol/L). Differences in body composition parameters were also measured and resulted in significant lower body weight, fat, and visceral fat in soy nuts group ($p<0.05$) while in tempeh group, only body weight and waist circumference were significantly decreased ($p<0.05$). This study suggested that daily consumption of soy nuts and tempeh containing 25g soy protein for six weeks showed a tendency to lower TC levels in hypercholesterolaemic-Indonesian participants. A more significant effect might be observed in subject with higher TC levels; and thus, further study is encouraged.

Keywords: body composition; hypercholesterolemia; soy nuts; tempeh; total cholesterol

ABSTRAK

Eksplorasi produk pangan dengan sifat penurun kolesterol sangat bermanfaat untuk menurunkan kejadian penyakit kardiovaskular pada mereka dengan hiperkolesterolemia. Studi intervensi ini melibatkan 42 peserta dengan kadar kolesterol total ≥4.92 mmol/L. Dua kelompok perlakuan diberikan 72gram kacang kedelai dan 66gram tempe per hari (25gram protein kedelai) selama enam minggu, sementara kelompok kontrol tidak. Kadar kolesterol total dan komposisi tubuh diukur sebelum dan setelah perlakuan pada semua kelompok. Penurunan kadar kolesterol total yang siginifikan (-0.85±0.82 mmol/L, $p<0.05$) teramati pada kelompok kacang kedelai dibandingkan dengan kontrol, sementara pada kelompok tempe, penurunan juga teramati meski tidak signifikan (-0.40±1.19 mmol/L). Perbaikan komposisi tubuh juga teramati secara signifikan pada parameter berat badan, lemak, dan angka lemak visceral pada kelompok kecang kedelai ($p<0.05$), sementara hanya parameter berat badan dan lingkar perut yang mengalami perbaikan signifikan pada kelompok tempe ($p<0.05$). Studi ini menyimpulkan bahwa konsumsi rutin kacang kedelai dan tempe sebesar 25gram protein kacang kedelai selama enam minggu cenderung dapat menurunkan kolesterol total pada orang Indonesia dengan kondisi hiperkolesterolemia. Bahkan penurunan kadar kolesterol total mungkin teramati lebih tinggi pada mereka yang memiliki kadar kolesterol total yang lebih tinggi sehingga diperlukan penelitian lebih lanjut.

Kata kunci: hiperkolesterolemia; kacang kedelai; kolesterol total; komposisi tubuh; tempe

Article Information

Article Type: Research Article
Journal Type: Open Access
Volume: 4 Issue 2

Manuscript ID
V4n21085-1

Received Date
27 July 2022

Accepted Date
11 January 2023

Published Date
28 February 2023

DOI: 10.33555/jffn.v4i2.100

Corresponding author:
Felicia Kartawidjajaputra
Jakarta, Indonesia, 13920
Email:
felicia@nutrifood.co.id

Citation:
Zulaikha, H.N., Muliadi, R.D., Kartawidjajaputra, F., Antono, L. 2023. Cholesterol-lowering Effect of Soy nuts and Tempeh on Hypercholesterolemic Subjects. J. Functional Food & Nutraceutical, 4(2), pp.95-102

INTRODUCTION

Hypercholesterolaemia is a condition that is characterised by elevated total cholesterol levels and/or low-density lipoprotein cholesterol (LDL-C) concentration; which can be defined as total cholesterol level >5.17 mmol/L and/or LDL-C level is >3.37 mmol/L (Gardner et al., 2001; Gebreegziabiher et al., 2021; Hu et al., 2021; Yudin et al., 2022). In most cases, hypercholesterolaemia is caused by interaction of sedentary lifestyle and an increased intake of saturated and trans-fatty acids (Ibrahim and Jialal, 2019; Martinez-Hervas and Ascaso, 2019). Without proper treatment and effort to improve the cholesterol levels, hypercholesterolaemia could increase the risk of cardiovascular disease (CVD). Amongst other risk factors, CVD is caused by elevated LDL levels since LDL is very vulnerable to oxidation due to its interaction with free radicals. If LDL gets oxidised, it becomes ox-LDL (oxidised LDL) which is atherogenic and will lead to CVD (Gao and Liu, 2017; Jaishankar et al., 2021). Based on the data from Health Ministry of Indonesia, in 2016, 21.2% of Indonesian citizens were diagnosed with hypercholesterolaemia (mostly from range 19 to 64 years old). This situation led to the increase of CVD cases, where the number of coronary heart disease case is the highest. The prevalence of coronary heart disease is 1.5% with mortality rate of 7.4 million (Kemenkes RI, 2018).

Maintaining normal blood cholesterol concentrations is important to reduce future CVD risk. Having healthier lifestyle by increasing physical activity and incorporating healthy diets, such as decreasing saturated fat and increasing the amount of fibre, into daily life is beneficial for health in general and helps reducing an elevated cholesterol levels (Mann et al., 2014). Research on healthy nutrition that could lower serum total cholesterol levels and promote cardiovascular health in general is growing. One such ingredient is soybean, which is well-known for its health benefit to lower serum total cholesterol and LDL-C levels (Cho et al., 2007; Ramdath et al., 2017). The cholesterol-lowering properties of soybean is supported by its several interesting compounds such as soy protein, isoflavones, and phytosterols. Several studies have indicated that those compounds contribute to the cholesterol-lowering properties of soybeans (Ramdath et al., 2017).

A study by Gardner et al., (2001) showed a significant reduction in total cholesterol and LDL-C concentrations after supplementation of 42 g soy protein, containing 80 mg aglycone isoflavones, in hypercholesterolaemic postmenopausal women. Meanwhile, a study by Bakhit et al., (1994) showed reduction of total cholesterol in hypercholesterolaemic participants; but, not in normocholesterolemic participants; after consumption of 25 g/d of soy protein for four weeks. A meta-analysis conducted by Jenkins et al., (2019) concluded that a daily intake of 25 g/day soy protein is recommended to have CVD risk improvement. It was postulated that the components responsible to cholesterol-lowering property of soybeans is its soy isoflavones (Montgomery, 2013). However, most studies mentioned that the beneficial effects could not be attributed solely to isoflavones since the source of isoflavones used is usually isolated soy protein (ISP). Thus, the beneficial effects could not be concluded because of the isoflavones solely since both soy protein and isoflavones were presented (Demonty et al., 2003).

Since most studies evaluating the effects of soy protein intake on lipid profile were using ISP, the effects of commercially available soy foods have not been fully evaluated. A recent study by Ruscica et al., (2018) evaluated the effects of whole soy foods intake (in the form of soy nuggets, soy burgers, soy desserts, and soy drinks) with 30 g soy protein contained. The results showed that the soy foods diet significantly improved plasma lipid profiles by reducing TC by 0.50 mmol/L and LDL-C by 0.38 mmol/L after 12 weeks intervention. In Indonesia, soy is widely consumed in the form of tempeh, a fermented soybean cake. However, the effect of soy nuts and tempeh consumption is rarely explored in Indonesia. Thus, in the present study, the objective is to evaluate the cholesterol-lowering effect of soy nuts and tempeh consumption containing 25 g soy protein for six weeks on hypercholesterolaemic Indonesian participants.

MATERIALS AND METHOD

Participants

Participants were employees of Nutrifood Indonesia, office branches of Jakarta and Ciawi. Men and women aged ≥20 years with TC levels of ≥4.92 mmol/L and willing to consume either soy nuts or tempeh sticks for 6 weeks according to the guidelines were eligible to participate in this study. The exclusion criteria were pregnant or breastfeeding woman; presented with a current or previous medical history for example cancer and other chronic disease; taking medication to interfere lipid or cholesterol metabolism; suffering gastrointestinal disease for which a high-fibre supplement would be contraindicated; suffering from cardiovascular disorder and/or heart disease; suffering from diabetes and/or hypertension; allergic to soy; taking regular prescribed medicine such as acetylcysteine which possible side effect is lipoprotein-lowering. Participants who eligible to join the study were informed not to consume any supplementation (including certain food such as fish oil, green tea extract, oat etc) to lower cholesterol intentionally during the study period. Informed consent forms were signed by all participants prior the start of the study. The study protocol was approved by ethical committee for medical research with registration number 0534 /III/LPPM.PM.10.05/04/2020.

There were 54 participants involved in this study and they were divided into three groups (control, tempeh, and soy nuts groups) based on their preference towards the sample to increase participants' compliance. However, due to COVID-19 outbreak, 12 participants were excluded due to difficulty during data collection. At the end, there were only 42 participants which completed the data for the study: three in control group, 18 in tempeh group, and 21 in soy nuts group.

Study design and data collection

This study was a non-randomised controlled study with three arms. Recruited participants were grouped into three groups: control group, soy nuts group, and tempeh group. This study took place for six weeks. Participants in control group were not given any sample, whereas participants in intervention groups were given 60 g/d and 72 g/d of tempeh sticks and soy nuts, respectively. Tempeh sticks were made by cut the tempeh obtained from local seller in Jakarta into small thin size and fried using air-fryer (200ºC, 8 mins). Soy nuts were made by soaking the soy nuts in water for one night then baked in the oven until the nuts dried and crunchy. Control group was chosen from participants who did not willing to consume the soy nut and tempeh and offered to be in control group. The provided sample given each day contained 25 g of soy protein, based on calculation from proximate analysis (analysis was done by MBRIO Food Laboratory and PT. Saraswanti Indo Genetech) result in Table 1.

Table 1. Nutrition Contents of Soy Nuts and Tempeh Sticks

Nutrients (%)	Tempeh sticks (per 60 g)	Soy nuts (per 72 g)
Total calorie	270.11 Kcal	303.09 Kcal
Protein	25 g	25 g
Carbohydrate	16.34 g	26.34 g
Fat	11.64 g	10.86 g
Fibre	8.58 g	11.82 g

At the beginning and the end of study period, participants' total cholesterol levels and body compositions were measured. TC levels were measured by commercial clinical laboratory (Prodia) at the beginning of the study using fresh venous blood. Meanwhile, at the end of the study, TC levels were measured using finger prick test device (EasyTouch GCU®, Taiwan) due to the COVID-19 pandemic that caused health public facilities to be temporarily restricted. Even though the method was different, finger prick test is also accurate and has good clinical utility and the difference is not significant (Sblendorio et al., 2008; Sedgwick et al., 2011; Loch et al., 2017). Participants' body compositions were measured using Omron Karada Scan, Japan at the beginning and at the end of the study.

Statistical analysis

Statistical analysis was performed with SPSS statistics software version 23 by IBM®, United States. Non-parametric analysis was chosen since the number of participants were less than 30 in each group. Baseline characteristics were checked to see if all the baseline data is homogenous (no

significant difference between the three groups) with Mann Whitney U Test. To test whether there was any significant change from baseline to end-treatment, Wilcoxon test was used. Finally, to evaluate if there were any significant difference between control and treatment group, Mann Whitney U Test was used. Significance for all analyses was set at $p<0.05$.

RESULTS AND DISCUSSION

Forty-two adults with elevated cholesterol (Female: 47.6%; Age 35.36 ± 9.33 years) completed this study. To detect a 0.39 mmol/L difference in TC, with an 80% power and SD of 0.23 mmol/L based on similar previous study by Bakhit et al., (1994), minimal of 14 participants each group were required for the study, yet the amount of control group will be explained in discussion.

Anthropometric characteristics and total cholesterol levels of the participants from baseline to end treatment are summarised in Table 2 (control vs soy nuts group) and Table 3 (control vs tempeh group). Wilcoxon test was conducted to see if there is any significant change from week 1 to week 6 for every parameter within each group. Table 2 and 3 show that there were no significant changes in control group after six weeks period of study.

Variations in study designs, the form of soy products, and the length of intervention might contribute to the results inconsistency (Wong et al., 1998). A meta-analysis indicated that supplementation with soy protein on hypercholesterolaemia participants would be resulted in significant reduction of TC levels only if the participants initially had TC levels ≥6.22 mmol/L and would not show a significant effect if the participants had initial TC levels of <5.15 mmol/L (Anderson et al., 1995; Wong et al., 1998; Wofford et al., 2012). Cholesterol-lowering effect of soy protein also seems to be low or negligible in normocholesterolemic participants. Another study also showed a non-significant result from soy protein supplementation towards hypercholesterolaemic participants with moderately elevated LDL-C levels (3.37-4.89 mmol/L) (Gardner et al., 2001). Nevertheless, minimum TC levels of the subject of our study was set to 4.92 mmol/L, since TC levels between 4.66-6.22 mmol/L were considered as borderline high thus needs attention and effort to be lowered (Jeong et al., 2018). Also, it was more recommended for people in borderline high TC levels (4.66-6.22 mmol/L) to improve the condition by having a healthier dietary intake and lifestyle rather than taking medication to lower cholesterol such as statin (Loch et al., 2017).

Table 2. Anthropometric Characteristics of Subjects in Control vs Soy Nuts Groups (Data are Means ± Standard Deviations)

Parameters	Control	Soy nuts	P-value *(Mann Whitney U test)*
Weight (Kg)	*N=3*	*N=18*	
Week 1	58.17 ± 12.29	66.54 ± 12.41	0.947
Week 6	56.70 ± 12.66	65.04 ± 12.43	0.356
Δ	-1.47 ± 1.37	-1.49 ± 0.78	0.814
P value (Wilcoxon test)	0.180	0.00	
Fat (%)	*N=3*	*N=18*	
Week 1	27.80 ± 10.61	27.54 ± 7.90	0.316
Week 6	27.37 ± 14.21	27.07 ± 7.79	0.887
Δ	-0.43 ± 1.36	-0.47 ± 0.89	0.669
P value (Wilcoxon test)	1.000	0.029	
Visceral Fat (%)	*N=3*	*N=18*	
Week 1	8.67 ± 5.80	8.19 ± 5.32	0.286
Week 6	8.33 ± 5.69	7.67 ± 5.21	0.740
Δ	-0.33 ± 0.76	-0.53 ± 0.32	0.814
P value (Wilcoxon test)	0.414	0.000	
Waist Circumference (cm)	*N=3*	*N=18*	
Week 1	81.17 ± 12.79	84.25 ± 9.17	0.658
Week 6	83.17 ± 12.86	83.07 ± 9.24	0.740
Δ	2.00 ± 5.68	-1.40 ± 4.48	0.307
P value (Wilcoxon test)	1.000	0.266	
Total Cholesterol (mmol/L)	*N=3*	*N=18*	
Week 1*	5.89 ± 0.60	5.73 ± 0.55	0.814
Week 6**	5.95 ± 0.35	4.89 ± 0.61	0.017
Δ	0.06 ± 0.90	-0.84 ± 0.82	0.185
P value (Wilcoxon test)	1.000	0.003	

*venous sampling
** capillary sampling

Participants in soy nuts group had a significant difference ($p<0.05$) in body weight (-1.49 ± 0.78 kg), body fat (-0.47 ± 0.89 %), and visceral fat (-0.53 ± 0.32 %), and total cholesterol level (-0.85±0.82 mmol/L) after 6 weeks treatment

compared to baseline. Meanwhile, participants in tempeh group had a significant difference ($p<0.05$) in body weight (-0.61 ± 0.98 kg) and waist circumference (-2.07 ± 3.71 cm) only. To further analyse the change (Δ) for 6 weeks period between control and soy nuts group; and between control and tempeh group, Mann Whitney U test was used. No significant result was obtained.

Table 3. Anthropometric Characteristics of Subjects in Control vs Tempeh Groups (Data are Means ± Standard Deviations)

Parameters	Control	Tempeh	P-value *(Mann Whitney U test)*
Weight (Kg)	*N=3*	*N=21*	
Week 1	58.17 ± 12.29	67.28 ± 9.17	0.506
Week 6	56.70 ± 12.66	66.67 ± 9.51	0.172
Δ	-1.47 ± 1.37	-0.61 ± 0.98	0.202
P value (Wilcoxon test)	0.180	0.013	
Body Fat (%)	*N=3*	*N=21*	
Week 1	27.80 ± 10.61	29.37 ± 5.61	0.158
Week 6	27.37 ± 14.21	29.04 ± 5.53	0.742
Δ	-0.43 ± 1.36	-0.32 ± 1.29	0.680
P value (Wilcoxon test)	1.000	0.313	
Visceral Fat (%)	*N=3*	*N=21*	
Week 1	8.67 ± 5.80	8.67 ± 4.48	0.387
Week 6	8.33 ± 5.69	8.76 ± 4.37	0.935
Δ	-0.33 ± 0.76	0.10 ± 1.01	0.505
P value (Wilcoxon test)	0.414	0.979	
Waist Circumference (cm)	*N=3*	*N=21*	
Week 1	81.17 ± 12.79	88.23 ± 8.07	0.877
Week 6	83.17 ± 12.86	86.16 ± 6.94	0.783
Δ	2.00 ± 5.68	-2.07 ± 3.71	0.238
P value (Wilcoxon test)	1.000	0.019	
Total Cholesterol (mmol/L)	*N=3*	*N=21*	
Week 1*	5.89 ± 0.60	5.91 ± 0.72	0.310
Week 6**	5.95 ± 0.35	5.43 ± 1.12	0.202
Δ	0.06 ± 0.90	-0.4 ± 1.19	0.505
P value (Wilcoxon test)	1.000	0.092	

*venous sampling
** capillary sampling

After the intervention, it was shown that TC levels after six weeks period of soy nuts and tempeh consumption were lower compared to the baseline. TC levels were significantly lower by -0.85±0.82 mmol/L at the end of the study in soy nuts group ($p<0.05$). Meanwhile in tempeh group, routine consumption of tempeh could decrease the TC level. In this study, there was a slight decrease by -0.40±1.19 mmol/L although this is statistically not significant ($p=0.09$). This reduction of TC levels was beneficial to help improving participants' TC levels into desirable level. These results would also be helpful in general for people with moderately-hypercholesterolaemia that consumption of soy food products with at least 25 g soy protein per day will have favourable effect to their TC levels. However, it must be noted that although there was a trend of lower TC levels observed after six weeks treatment, these changes in TC levels were not significantly different compared to the control group.

Besides the TC levels, body parameters were also measured. In soy nuts group, participants' weight, body fat, and visceral fat were significantly lower after six weeks ($p<0.05$). Meanwhile in tempeh group, only the participants' weight and waist circumference were significantly lower ($p<0.05$) at the end of the study. Participants' protein intake was recorded using food dairy to make sure that any changes are due to the soy protein and not from other foods (Table 4). It was shown that there was no significant difference between groups and between baselines to end-treatment; and implying that the results were due to our treatments during study period. Even though it was not significant, the average of protein consumption was higher in tempeh and soy nuts group due to the soy protein than was added to their daily food consumption compared with control group.

Table 4. Food Diary for Protein Consumption (Data are Means ± Standard Deviations)

Parameters	Control	Tempeh	Soy Nuts	P-value *(Mann Whitney U test)*
Protein (g)	*N=3*	*N=21*	*N=18*	
Week 1	55.33 ± 26.96	72.13 ± 12.08	68.87 ± 16.01	0.436
Week 6	52.67 ± 6.08	68.79 ± 11.79	63.29 ± 15.56	0.056
Δ	-2.67 ± 23.25	-3.33 ± 17.21	-5.59 ± 17.07	0.829
P value (Wilcoxon test)	1.000	0.484	0.154	

One of limitations to our study was the difference of TC levels measurement methods between baseline and end treatment that could be subject to validity. TC levels measurement in this study was different between baseline and end-treatment due to the outbreak situation. This study used venous sampling in baseline and capillary sampling (prick test) in end-treatment. Although the blood-

sampling method was different between baseline and end-treatment (venous vs capillary blood), Sblendrio et al., (2008) and Sedgwick et al., (2011) concluded that capillary and venous blood lipid concentration were not significantly different. The other limitation was the amount of control group which only three participants had completed the study due to COVID-19 pandemic.

In addition, a comparative study between measurements of serum cholesterol by laboratory and by finger-prick test was conducted by Abdelmotaleb et al., (2017). The study concluded that EasyTouch® GCU is a promising device for quick and accurate total cholesterol measurement with there was no significant difference compared to laboratory test (0.01 mmol/L lower than laboratory test). Nonetheless, methods in research should be consistent and remain the same from the beginning until the end of the study. Another limitation of this clinical trial was the lack of measurement regarding soy phytosterol, isoflavones, and proteins in soy nuts and tempeh. The equol production in the gut, an active metabolite of soy isoflavone daidzein could bind estrogen receptors which associated with lipid-lowering efficacy (Simental-Mendia et al., 2018; Alshehri et al., 2021). Soy isoflavone also could serve as ligands for lipid-regulating proteins, such as liver X receptor, farnesoid X receptor and peroxisome proliferator activated receptors (PPARs), which would decrease hepatic lipid synthesis, bile acid synthesis, and cholesterol reabsorption (Ramdath et al., 2017). The other components are soy proteins such as 7S and 11S globulin. These proteins could regulate LDLR activity and inhibit hepatic ApoB synthesis (Mejia et al., 2019; Caponio et al., 2021). Measurement on phytosterol, isoflavones, and peptides contained in soy nuts and tempeh might explain the effect exhibited in the future studies.

CONCLUSION

This study showed that daily consumption of soy nuts and tempeh containing 25 g soy protein for six weeks had the tendency to lower TC levels in hypercholesterolaemic-Indonesian participants. Although the decrease in TC level after soy nuts and tempeh consumption in this study was not different significantly from control group, significant lower TC levels observed between the baseline to end-treatment should not be just ignored. Thus, daily soy nuts and tempeh consumption could be incorporated as part of healthy lifestyle recommendation for people with hypercholesterolaemia in attempt to reduce their TC levels.

ACKNOWLEDGEMENT

This study was fully funded by PT. Nutrifood Indonesia. We thank Joghum Plat for his advice. We appreciate Syauqi, Putri and Laurent for their help during the study.

CONFLICT OF INTEREST

Authors 2-4 are the employees of PT Nutrifood Indonesia. Yet, the funder had no role in study design, data collection, analysis and interpretation.

REFERENCES

Abdelmotaleb, G. S., Abdelmonaem, E. R., Ahmed, E. S. and Aboelsoued, A. 2017. Comparative study between measurements of serum choles terol, uric acid, and glucose in children with β-thalassemia by laboratory and bedside methods. *International Journal of Advanced Research.* 5(6), pp.963-973.

Alshehri, M. M., Sharifi-Rad, J., Herrera-Bravo, J., Jara, E. L., Salazar, L. A., Kregjel, D., Uprety, Y., Akram, M., Iqbal, M., Martotell, M., Torrens-Mas, M., Pons, D. G., Dastan, S. D., Cruz-Martins, N., Ozdemir, F. A., Kumar, M. and Cho, W. C. 2021.Therapeutic potential of isoflavones with an emphasis on daidzein. *Oxidative Medicine and Cellular Longevity*. 6331630, pp.1-15.

Anderson, J. W., Johnstone, B. M. and Cook-Newell M. E. 1995. Meta-analysis of the effects of soy protein intake on serum lipids. *New England Journal of Medicine.* 333(5), pp.276-282.

Bakhit, R. M., Klein, B. P., Essex-Sorlie, D., Ham, J. O., Erdman Jr, J. W. and Potter, S. M. 1994. Intake of 25 g of soybean protein with

or without soybean fiber alters plasma lipids in men with elevated cholesterol concentrations. *The Journal of Nutrition*. 124(2), pp.213-222.

Caponio, G. R., Wang, D. Q., Di Ciaula, A., De Angelis, M. and Portincasa, P. 2021. Regulation of cholesterol metabolism by bioactive components of soy proteins: novel translational evidence. *International Journal of Molecular Sciences.* 22(227), pp.1-18.

Cho, S. J., Juillerat, M. A. and Lee, C. H. 2007. Cholesterol lowering mechanism of soybean protein hydrolysate. *Journal of Agricultural and Food Chemistry*. 55(26), pp.10599-10604.

Demonty, I., Lamarche, B. and Jones, P. J. 2003. Role of isoflavones in the hypocholesterolemic effect of soy. *Nutrition Reviews.* 61(6), pp.189-203.

Gardner, C. D., Newell, K. A., Cherin, R. and Haskell, W. L. 2001. The effect of soy protein with or without isoflavones relative to milk protein on plasma lipids in hypercholesterolemic postmenopausal women. *The American Journal of Clinical Nutrition*. 73(4), pp.728-735.

Gao, S. and Liu, J. 2017. Association between circulating oxidized low-density lipoprotein and atherosclerotic cardiovascular disease. *Chronic Diseases and Translational Medicine*. 3(2), pp.89-94.

Gebreegziabiher, G., Belachew, T., Mehari, K. and Tamiru, D. 2021. Prevalence of dyslipidemia and associated risk factors among adult residents of Mekelle City, Northern Ethiopia. *PLoS ONE*. 16(2), e0243103.

Hu, E.A., Scharen, J., Nguyen, V. and Langheier, J. 2021. Evaluating the impact of a digital nutrition platform on cholesterol levels in users with dyslipidemia: longitudinal study. *JMIR Cardio*. 5(1), e28392.

Ibrahim, M. A. and Jialal, I. 2019. Hypercholesterolemia StatPearls [Internet]: StatPearls Publishing.

Jaishankar, T., Shivasekar, M. and Vinodhini, V. M. 2021. The Effect of Circulating Oxidized LDL and High Sensitivity C-Reactive Protein on Coronary Heart Disease Susceptibility in a South Indian Population. *Biomedical and Pharmacology Journal*. 14(3), pp. 1427-1434.

Jenkins, D. J., Blanco, M. S, Chiavaroli, L., Viguiliouk, E., Li, S. S. and Kendall, C. W. 2019. Cumulative Meta-Analysis of the Soy Effect Over Time. *Journal of the American Heart Association.* 8(13), e012458.

Jeong, S. M., Choi, S., Kim, K., Kim, S. M., Lee, G. and Park, S. Y. 2018. Effect of change in total cholesterol levels on cardiovascular disease among young adults. *Journal of the American Heart Association*. 7(12), e008819.

Kemenkes R. 2018. Hasil utama RISKESDAS 2018. [Online]. [Accessed 20 June 2021]. Available from: http://www depkes go id/resources/download/info-terkini/materi_rakorpop_2018/Hasil% 20Riskesdas.

Loch, A., Bewersdorf, J. P., Kofink, D., Ismail, D., Abidin, I. Z. and Veriah, R. S. 2017. Generic atorvastatin is as effective as the brand-name drug (LIPITOR®) in lowering cholesterol levels: a cross-sectional retrospective cohort study. *BMC Research Notes.* 10(1), pp.291.

Mann, S., Beedie, C. and Jimenez, A. 2014. Differential effects of aerobic exercise, resistance training and combined exercise modalities on cholesterol and the lipid profile: review, synthesis and recommendations. *Sports Medicine*. 44(2), pp.211-221.

Martinez-Hervas, S. and Ascaso, J. F., 2019. Hypercholesterolemia. In: Huhtaniemi, I., Martini, L. ed. *Encyclopedia of Endocrine Diseases*. 2nd ed. Cambridge: Academic Press, pp.320-326.

Mejia, S. B., Messina, M., Li, S. S.,Viguiliouk, E., Chiavaroli, L., Khan, T. A., Srichaikul, K., Mirrahimi, A., Sievenpiper, J. L., Kris-

Etherton, P. and Jenkins, D. J. A. 2019 . A meta-analysis of 46 studies identified by the FDA demonstrates that soy protein decreases circulating LDL and total cholesterol concentrations in adults. *The Journal of Nutrition.* 0, pp. 1-14.

Montgomery, K. S. 2003. Soy protein. *The Journal of Perinatal Education*. 12(3), pp.42-45.

Ramdath, D. D., Padhi, E. M., Sarfaraz, S., Renwick, S. and Duncan, A. M. 2017. Beyond the cholesterol-lowering effect of soy protein: a review of the effects of dietary soy and its constituents on risk factors for cardiovascular disease. *Nutrients.* 9(4), pp.324.

Ruscica, M., Pavanello, C., Gandini, S., Gomaraschi, M., Vitali, C. and Macchi, C. 2018. Effect of soy on metabolic syndrome and cardiovascular risk factors: a randomized controlled trial. *European Journal of Nutrition.* 57(2), pp.499-511.

Sblendorio, V., Palmieri, B. and Riccioni, G. 2008. Blood cholesterol concentration measured by CR3000: fingerstick versus venous sampling. *International Journal of Immunopathology and Pharmacology*. 21(3), pp.729-733.

Sedgwick, M. J., Morris, J. G., Nevill, M. E. and Barrett, L. A. 2011. Comparison of lipid and lipoprotein concentrations obtained when using capillary and venous plasma. *Atherosclerosis.* 218(2), e10.

Simental-Mendía, L. E., Gotto, A. M., Atkin, S. L., Banach, M., Pirro, M. and Sahebkar, A. 2018. Effect of soy isoflavone supplementation on plasma lipoprotein(a) concentrations: a meta-analysis. *Journal of Clinical Lipidology*. 12(1), pp.16–24. Wofford, M., Rebholz, C., Reynolds, K., Chen, J., Chen, C. and Myers, L. 2012. Effect of soy and milk protein supplementation on serum lipid levels: a randomized controlled trial. *European Journal of Clinical Nutrition.* 66(4), pp.419-425.

Wong, W. W., Smith, E., Stuff, J. E., Hachey, D. L., Heird, W. C. and Pownell, H. J. 1998 Cholesterol-lowering effect of soy protein in normocholesterolemic and hypercholesterolemic men. *The American Journal of Clinical Nutrition.* 68(6), 1385S-9S.

Yudin, R., Aman, A., Rasyid, H., Bakri, S., Sanusi, H., Daud, N. and Zainuddin, A. 2022. Risk of dyslipidemia in obese young adult subjects as measured by various obesity indices. *Journal of Endocrinology and Metabolism*. 12(3), pp.102-106.