ORIGINAL ARTICLE

The Potential Effect of Sweet Potato (*Ipomoea Batatas L.*) Extract On Total Cholesterol and Low Density Lipoprotein (LDL) In Hypercholesterol-Model Wistar Rat (*Rattus norvegicus)*

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ABSTRACT

Introduction: CHD has high development among 86% in the world with the prevalence in urban (0.6%) than rural (0.4 %) areas. Atherosclerosis is an inflammatory response in blood vessels due to hypercholesterolemia and oxidized LDL. LDL and total cholesterol levels can be reduced by anthocyanins compounds, which are contained in purple sweet potato (*Ipomoea batatas L.*) This study aimed to determine the effectiveness of purple sweet potato extract in reducing total cholesterol and LDL.
Methods: This study was a post-test-only control group experimental design. Twenty-five Wistar rats were divided into five groups: normal control, negative control, and three treatment groups fed by purple sweet potato extract doses of 66.67, 133.33, and 266.67 mg/kg BW/day.
Results: Based on the statistical analysis there were significant differences between the treatment group and control groups. The highest dose of purple sweet potato extract (266.67 mg/kg BW/day) has an optimal effect in decreasing total cholesterol and LDL levels.
Conclusion: Purple sweet potato extract (266.67 mg/kg BW/day) can reduce total cholesterol and LDL levels of Wistar Rats.

Introduction

CHD is one of disease that has a high mortality rate in the world. According to WHO, heart disease is common in low and middle-income countries. A study reported that 86% of CHD cases were emerged in developing and third-world countries.[1] One of country that has high prevalence of CHD is Indonesia. The age group between 65-74 years old have the highest risk of CHD. The CHD risk decreases slightly for someone older than 75 years old. The prevalence of CHD is higher in urban (0.6%) than rural (0.4 %) areas.[2] CHD is a development result of the formation of atherosclerosis, that can occur during childhood and gets thicker over time. Atherosclerotic forms plaques in response to the injured endothelial wall.[3] The endothelial dysfunction occurs early in atherogenesis and allows lipoproteins to accumulate in the intima.[4]

Atherosclerosis is thickening or hardening of the arteries caused by a buildup of plaque in the inner lining of an artery. As a response to inflammation in blood vessels, atherosclerosis is a progressive. It initiated by mass deposits of collagen, fat, cholesterol, and indicated by myocyte proliferation. Atherosclerosis can lead to coronary heart disease (CHD).[5] Endothelial injury initiated by several factors, such as hypercholesterolemia, oxidized low-density lipoprotein (LDL), hypertension, smoking habit, diabetes, obesity, homocysteine, high saturated fat diet, and cholesterol.[6,7] Hypercholesterolemia may be initiated by high cholesterol intake.[8] The LDL fraction in hypercholesterolemia is the most important factor of atherosclerosis formation.[9]

Many study reported the alternative medicine from plants that may prevent atherosclerosis.10 One of them is purple sweet potato (*Ipomoea batatas L.*).[11] Despite its nutritious potential, there are lack purple sweet potato

production for culinary or medicine purpose. Purple sweet potato has a high anthocyanin, about 110-210 mg per 100 grams.[12] Anthocyanin, belong to antioxidants,[13] is a chemical property to prevent cancer, aging, and degenerative diseases such as atherosclerosis. Anthocyanin also serves as antimutagenic, anticarcinogenic, prevents liver dysfunction, antihypertensives, and lowers blood sugar levels (antihyperglycemic).[14,15] Anthocyanin also has potential activity to lower LDL level through AMPK pathway.[16,17]

Because of the potential atherosclerosis prevention ability in purple sweet potato; therefore, we tried to elucidate whether the antioxidant properties of purple sweet potato (*Ipomea batatas L.*) can lower total cholesterol and LDL level in atherosclerosis-model Wistar rats.

Methods

This study used the Post-test only Control Group design. The post-test study model design was applied to avoid the rat's trauma and stress to the treatment effect. Stress rats can change fat metabolism in rats that making the resulting bias or invalid. Therefore, to prevent this condition, we used negative controls that were fed as normal rats or pre-treated rats.

The purple sweet potato (*Ipomea batatas L.*) used was a clone of MSU 03028-10, which was cultivated organically and extracted with doses of 66.670, 133.330, and 266.67 0mg/kg BW in each treatment group.[9] Wistar rats were divided into five experimental groups, five rats each. The normal control group was fed normally for 56 days or 8 weeks. Negative control (rats fed by hypercholesterolemic diet for 56 days or 8 weeks). IB1 (hypercholesterolemic diet and 66.670 mg/kg BW purple sweet potato extract). IB2 (hypercholesterolemic diet and 133.330 mg/kg BW purple sweet potato extract). IB3 (hypercholesterolemic diet and 266.67 mg/kg BW purple sweet potato extract). The treatment groups were fed with the hypercholesterolemic diet from the first to the seventh day. In the eight days, the treatment groups were fed purple sweet potato extract until the 63rd day. This research has ethical registration number 482-KEP-UB.

Hypercholesterolemic Diet

The hypercholesterolemic diet consisted of the Comfeed PAR-s flour, 5% duck egg yolk, cholic acid, pork oil, 10% goat oil (40 grams). The treatment groups were fed the hypercholesterolemic diet for 7 days, while the negative control group for 56 days or 8 weeks.

Purple Sweet Potato Extraction

The purple sweet potato was washed and cut into 2-2.5 cm, then dried inside the oven at 80° C. The dried sweet potato was mashed to obtain the powder. A total of 100 grams of purple sweet potato powder was then mixed with 900 ml ethanol and homogenized for 30 minutes. After sedimented overnight, the mixture then evaporated. The evaporated product was stored in the freezer until further use.

Anesthetic Process

The anesthetic process was carried out by inserting the rats into a glass jar filled with cotton mixed with chloroform. Anesthesia was carried out by inhalation with ± 0.67 ml ether per rat for ± 60 seconds, which was calculated using a stopwatch.

Blood Isolation Process

After the rats were unconscious due to anesthesia, the rats were placed on an examination table. Then rat blood (± 3 ml) was collected from the left ventricle with a syringe for further analysis.

Statistical Analysis

The data were analyzed using SPSS 12. Data were analyzed using one-way ANOVA to determine the significant difference between the control and the treatment samples ($p<0.01$). After that, the data were analyzed using a Post-hoc test to determine the significant difference between the control samples and the treatment samples. The correlation test was used to determine the significant effect between purple sweet potatoes doses and reduction of cholesterol total and LDL, and regression tests were used to determine the correlation in between.

Results

Studies have found that purple sweet potato has high anthocyanin content. Various purple sweet potatoes have different amounts of anthocyanin content, while the MSU 03028-10 variety has a total anthocyanin of 1,583.71 mg/100 gram.9 The high levels of anthocyanins in this variety have the potential as alternative herbs to lower blood cholesterol and LDL levels. Anthocyanins function in preventing oxidative stress with the recommended daily requirement of 180-215 mg/day.

In this study, the increase in LDL and cholesterol levels in rats after being fed a high-fat In this study, the increase in LDL and cholesterol levels in rats after being fed a high-fat diet was presented in Tables 1 and 2 (negative samples compared to normal samples).

Table 1. Descriptive distribution of LDL

	N	Mean
Normal	5	11.400 ± 1.140
Negative	5	23.400 ± 2.302
IB1	5	16.600 ± 1.673
IB2	5	15.600 ± 1.140
IB3	5	12.200 ± 1.304

Based on table 1 the use of treatment was able to significantly increase LDL results in the negative group. The LDL value in the negative group was 23.40 which had a significant difference with the normal group ($p<0.05$). IB1 (16.60) and IB2 (15.60) both had no significant difference but had a significant difference when compared to the control group ($p<0.05$). The treatment group at IB3 (11.40) did not have a significant difference when compared to the normal group. This indicates that the IB3 treatment group is effective in lowering LDL to return to normal conditions.

Table 2. Descriptive Distribution of Total Cholesterol

	N	Mean
Normal	5	58.800 ± 1.789a
Negative	5	80.800± 1.924b
IB1	5	73.800 ± 0.837c
IB2	5	69.600 ± 2.074d
IB3	5	63.400 ± 1.517e

Based on table 2 the use of treatment was able to significantly increase total cholesterol in the negative group. The total cholesterol value in the negative group, which was 80.80, had a significant difference with the normal group ($p<0.01$). IB1 (73.800), 1B2 (69.600) and IB3 (63.400) each had a significant difference when compared to the normal and negative group ($p<0.01$). This indicates that the use of treatment affects all treatment groups and is the most effective was the treatment group at IB3 which was able to reduce total cholesterol close to normal conditions.

The extract of purple sweet potato had a significant effect of LDL and total cholesterol in rat models ($p<0.01$) (Table 1 and table 2). As the high-fat fed experimental group, IB1, IB2, dan IB3 were assumed to have high cholesterol and LDL level. However, the cholesterol and LDL level in experimental group was reduced by the purple sweet potato extract administration.

This study confirms that decreased cholesterol and LDL levels occurred at the negative control sample after the extract administration. From all the experimental doses, purple sweet potato dose of 266.67 mg/kg BW has the highest cholesterol and LDL levels reduction in IB3 (Table 1; IB3).

Discussion

The anthocyanin reduces cholesterol and LDL levels by activating the adenosine-monophosphate protein kinase (AMPK) pathway. It inhibits the HMG-CoA reductase enzyme in cholesterol synthesis. When the cholesterol formation is inhibited, VLDL will not be hydrolyzed and LDL will be suppressed.16,17,19 Other study also reported that water extract of purple sweet potato has exogenous antioxidant activity to lower MDA levels in the blood, liver, heart, and intestines.[14,20]

Based on Tables 1 and 2, the higher doses of the purple sweet potato, can reduce the LDL and cholesterol levels more significantly. It indicates that purple sweet potato has potential to reduce cholesterol and LDL levels to inhibit atherosclerosis. Purple sweet potato can disrupt the formation of cholesterol and LDL in hypercholesterolemic rat blood. [21,22] Purple sweet potato contains anthocyanin, ascorbic acid, and beta-glucan that increase high density lipoprotein (HDL) concentrations to suppress LDL formation. This effect may partially be mediated through the inhibition of cholesterol ester transfer protein (CETP).[23,24]

The best result cholesterol and LDL inhibition obtained by purple sweet potato extract dose 266.67 mg/kg BW. It confirms that recommended daily intake of purple sweet potato as nutritional food or supplement can prevent atherosclerosis due to increasing cholesterol and LDL levels.

Conclusion

Sweet potato extracts (Ipoema batatas L.) effectively reduced total cholesterol and LDL levels. The highest dose of 266.67 mg/kg BW is the most significant in reducing cholesterol and LDL levels in hypercholesterolemic Wistar rat. This study report demonstrates that purple sweet potato is a promising alternative food source that should be included in healthy diet to prevent atherosclerosis.

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Conflict of Interest

All authors declare that they have no conflict of interest.

References

1. World Health Organization. Cardiovascular diseases (CVDs), https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (2021, accessed 22 March 2022).
2. Indonesia Health Ministry. Laporan Hasil Riset Kesehatan Dasar, https://www.litbang.kemkes.go.id/laporan-riset-kesehatan-dasar-riskesdas/ (2018, accessed 12 March 2022).
3. Bentzon JF, Otsuka F, Virmani R, et al. Mechanisms of Plaque Formation and Rupture. Circ Res 2014; 114: 1852–1866.
4. Rafieian-Kopaei M, Setorki M, Doudi M, et al. Atherosclerosis: Process, indicators, risk factors and new hopes. Int J Prev Med 2014; 5: 927–946.
5. Liao K-W, Lin C-S, Chen WL, et al. Antibodies against Helicobacter pylori heat shock protein 60 aggravate HSP60-mediated proinflammatory responses. Cytokine 2011; 55: 174–180.
6. Mahan LK, Escott-Stump S, Krause M V, et al. Krause's Food \& Nutrition Therapy. Saunders/Elsevier, https://books.google.co.id/books?id=fgadSQAACAAJ (2008).
7. Sun HJ, Wu ZY, Nie XW, et al. Role of endothelial dysfunction in cardiovascular diseases: The link between inflammation and hydrogen sulfide. Front Pharmacol 2020; 10: 1–15.
8. Mytilinaiou M, Kyrou I, Khan M, et al. Familial Hypercholesterolemia: New Horizons for Diagnosis and Effective Management. Front Pharmacol; 9. Epub ahead of print 2018. https://doi.org/10.3389/fphar.2018.00707.
9. Libby P, Buring JE, Badimon L, et al. Atherosclerosis. Nat Rev Dis Prim 2019; 5: 56.
10. Kirichenko T V, Sukhorukov VN, Markin AM, et al. Medicinal Plants as a Potential and Successful Treatment Option in the Context of Atherosclerosis. Front Pharmacol 2020; 11: 403.
11. Setiawan M, Putra ST, Sargowo D. Efficacy of purple sweet potato (Ipomoea batatas) extract to prevent the aortic wall thickness of white male rats atherosclerosis model. Med Plants 2019; 11: 55–59.
12. M.Mónica Giusti REW. Characterization and Measurement of Anthocyanins by UV-Visible Spectroscopy. Curr Protoc Food Anal Chem. Epub ahead of print 2001. https://doi.org/10.1002/0471142913.faf0102s00.
13. Craig WJ. Phytochemicals: guardians of our health. J Am Diet Assoc 1997; 97: S199-204.
14. Amagloh FC, Yada B, Tumuhimbise GA, et al. The potential of sweetpotato as a functional food in sub-saharan africa and its implications for health: A review. Molecules 2021; 26: 1–21.
15. Mattioli R, Francioso A, Mosca L, et al. Anthocyanins: A Comprehensive Review of Their Chemical Properties and Health Effects on Cardiovascular and Neurodegenerative Diseases. Molecules 2020; 9(707). https://doi.org/10.3390/molecules25173809.
16. Ju R, Zheng S, Luo H, et al. Purple Sweet Potato Attenuate Weight Gain in High Fat Diet Induced Obese Mice. J Food Sci 2017; 82: 787–793.
17. Wallace TC, Slavin M, Frankenfeld CL. Systematic Review of Anthocyanins and Markers of Cardiovascular Disease. Nutrients; 8. Epub ahead of print January 2016. https://doi.org/10.3390/nu8010032.
18. Bach D, Bedin AC, Lacerda LG, et al. Sweet Potato (Ipomoea batatas L.): a Versatile Raw Material for the Food Industry. Brazilian Arch Biol Technol 2021; 64: 1–14.
19. Reis JF, Monteiro VVS, de Souza Gomes R, et al. Action mechanism and cardiovascular effect of anthocyanins: a systematic review of animal and human studies. J Transl Med 2016; 14: 315.
20. Klinger ACK, Toledo GSP, Robalo S, et al. Cholesterol-lowering effect of diet with added sweet potato (Ipomea batatas) vines in rabbits. Archivos Latinoamericanos de Nutricion 2018; 68: 211–216.
21. Yadnya TGB, Sudana IB, Mahardika IG, Mastika IM. The effect of fermented purple sweet potato (Ipomoea batatas l) in the ration on the antioxidant profile and meat cholesterol of bali duck. J Chem Inf Model 2013; 53: 1689–1699.

22. Sutirta-Yasa IWP, Jawi IM. Antioxidant potential and hypolipidemic effects of combined purple sweet potato (Ipomoea batatas L.) tuber extract with honey in rats given high cholesterol feed. Bali Med J 2017; 6: 65.
23. Xu Z, Xie J, Zhang H, et al. Anthocyanin supplementation at different doses improves cholesterol efflux capacity in subjects with dyslipidemia--a randomized controlled trial. Eur J Clin Nutr 2021; 75: 345+.
24. Chang H-H, Lan Y-C, Chung S-D, et al. Sweet Potato Leaf Feeding Decreases Cholesterol, Oxidative Stress and Thrombosis Formation in Syrian Hamsters with a High-Cholesterol Diet. Life (Basel, Switzerland); 11. Epub ahead of print August 2021. https://doi.org/10.3390/life11080802.