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Research

The Effects of Ethanol Extract, Chayote (*Sechium Edule* (Jacq.) Swartz) Fraction and Juice on the High-density Lipoprotein Level in Male White Mice

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ABSTRACT

Background: Cholesterol imbalance occurs in Diabetes Mellitus, where high-density lipoprotein (HDL) levels are low and low-density lipoprotein (LDL) increases, where this imbalance results in the appearance of atherosclerosis. HDL has antiarterosclerotic potential so it needs to be targeted for therapy. One of the bioactive compounds that have this effect is found in chayote (*Sechium edule* (Jacq.) Swartz). This study aimed to examine the effects of ethanol extract, Chayote (*Sechium Edule* (Jacq.) Swartz) fraction and juice on the HDL level in male white mice

Subjects and Method: A randomized controlled trial study was conducted to test HDL level in 54 male white rats of the Wistar strain (*Rattus novergius sp.*) after received ethanol extract, Chayote (*Sechium Edule (Jacq.) Swartz*) fraction and juice. The dependent variable was the HDL level. The independent variable was the variation in the dose of ethanol extract, fraction and *Sechium edule* (*Jacq.) Swartz* Juice. The data were analyzed using Anova test.

Results: The treatment group induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg/kgBW) + HFD and obtained ethanol extract of chayote fruit 150 mg / kgBW, orally had the highest average HDL levels compared to other groups (Mean = 17.31; SD = 3.14).

Conclusion: The ethanol solvent found in the ethanol extract is better because it attracts biaoctive compounds so that it has a better effect than the ethyl acetate fraction and the n-hexane fraction.

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Keywords: HDL, Flavonoid, *Sechium edule (Jacq.) Swartz*

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BACKGROUND

Diabetes mellitus (DM) is a risk factor for atherosclerosis which can lead to complications of heart disease. Atherosclerosis is caused by high blood fat low-density lipoprotein (LDL) while high-density lipoprotein (HDL) is low (Farbstein and Levy, 2012). Atherogenic dyslipidemia in diabetes is characterized by increased concentrations of TG-rich lipoproteins (TRLs), small dense Low Density Lipoproteins (sd-LDL), decreased HDL concentrations in serum (Hirano T, 2018). In DM, there are 2 important pathways that cause atherosclerosis, namely hyperglycemia and insulin resistance, secondly dyslipidemia. Both of these pathways will induce oxidative stress and inflammation which affects the endothelial dysfunction of blood vessels, which will then develop into atherosclerotic lesions (Poznyak et al., 2020).

HDL has an important role as antiatherogenic, carrying cholesterol from the periphery to the liver, anti-inflammatory by inhibiting TNF-α (tumor necrosis factor-α) and IL-1 (interleukin 1) stimuli, antithrombotic, antiapoptotic, antioxidant, vasodilator, and repairing vessel endothelium, blood, glucose homeostasis (Barter, 2011; Farbstein and Levy, 2012; Younis and Durrington, 2012; Femlak et al., 2017). HDL dysfunction in DM occurs due to the state of insulin resistance inactivating lipolytic enzyme lipoprotein lipase (LPL) thereby reducing triglyceride hydrolysis (TG), cholesteryl ester transfer protein (CETP) induces HDL catabolism, and increased hepatic triglyceride lipase (HTGL) activity causes HDL clearance to also increase (Bjornstad and Eckel, 2018).

This reduction in HDL levels can be prevented by administering flavonoids including Isoflavones, anthocuanidins, flavanols, flavonols, flavones and flavanones. The mechanism of action is by increasing the activity of Paraoxonase 1 (PON1) by preventing modification of LDL and the main component of HDL antiarterosclerosis (Tavori et al., 2010; Millar et al., 2017). One of these flavonoids can be found in the *Sechium edule (Jacq.) Swartz* chayote. A study by Siahaan et al. (2019), shows that the flavonoids in chayote have antihypertriglyceride, antiobesity, antihyperglycemia and antioxidant effects. In addition, the polyphenol extract of the chayote root of *Sechium edule (Jacq.) Swartz* promoted lipogenesis and stimulated lipolysis by activating signal AMP-activating protein kinase (AMPK) on HepG2 cells (Wu, et al., 2014). Its biological effect is cardioprotective by increasing HDL and reducing VLDL, LDL, total cholesterol, triglycerides, serum transminase, alkaline phosphatase, lactate dehydrogenase, creatinine kinase (Vieira et al., 2018). In this study, the authors tried to examine the effectiveness of ethanol extract, fractions and Sechium edule (Jacq.) Swartz juice on HDL levels.

SUBJECTS AND METHOD

1. Study Design

This study used a pure experimental research type with the post test method randomized controlled group design.

2. Population and Sample

The experimental animals used in this study were white male Wistar rats, aged 2.5 - 3 months, body weight 180-220 grams and healthy. The selection of mice as experimental animals is based on the consideration that genetically, rats have similarities to humans and have the ability to adapt to the laboratory environment. The sample allocation (grouping) of experimental animals used simple random sampling. The sample size was estimated using Federer's formula, each group using 3 male white rats Wistar (Rattus novergius sp.)

With 18 groups of treatment groups so that the total number of the study sample was 54. Chayote was done using purposive sampling method, which is taken from the yard of the Sidamanik residents.

3. Study Variables

The dependent variable was HDL level. The independent variables were variation dose of ethanol extract, *Sechium edule* (Jacq.) Swartz fraction and juice.

4. Operational Definition of Variables

HDL level is the result of blood serum spectrophotometer examination using a diagnostic spectrum reagent.

5. Study Instruments

HDL examination was carried out in an integrated laboratory at the Faculty of Medicine, University of North Sumatra, using the Spectrophotometric method with spectrum diagnostic reagents.

6. Data Analysis

HDL levels after received ethanol extract, *Sechium edule* (Jacq.) Swartz fraction and juice were analyzed by using Anova test.

RESULTS

HDL levels were measured after 21 days of administering the extract, fraction and juice of *Sechium edule* (Jacq.) Swartz and compared with the control group as shown in Table 1.

From Table 1, it was found that the highest HLD content was found in group G which was given chayote fruit ethanol extract 150 mg/ kgBW per oral, while the lowest HLD level was found in group O which was given chayote juice 100 mg/ KgBW per oral with <0.001, which means there is a meaningful relationship.

Table 1. HDL levels of Wistar male white rats (*Rattus novergius sp.*)

Group	Level of HDL		p
	Mean	SD	
1	18.13	1.74	
2	25.16	8.08	
3	14.41	1.72	
4	7.50	2.20	
5	10.50	6.82	
6	9.70	2.09	
7	**17.31**	**3.14**	
8	13.04	6.50	
9	9.78	1.46	<0.001
10	8.06	1.50	
11	6.24	1.92	
12	7.46	2.40	
13	7.18	1.02	
14	8.91	1.54	
15	**5.80**	**2.27**	
16	7.64	1.57	
17	7.15	1.11	
18	6.40	1.72	

Note:

a. Group 1, negative control (normal) was not given any treatment, like normal rats in general who were given excessive food and drink (ad libitum) in their cages.
b. group 2, positive control, induced Streptozotocin 50 mg / kgBW + HFD
c. group 3, Positive control, induced nicotinamide (120 mg / kg) + HFD
d. group 4, Positive control, induced Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD
e. group 5, the treatment group induced by Streptozotocin 50 mg / kgBW + nicotinamide (120

mg / kg) + HFD, with ethanol extract of chayote fruit 50 mg / kgBW, p.o.
f. group 6, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with ethanol extract of chayote fruit 100 mg / kgBW, p.o.
g. group 7, the treatment group which was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with ethanol extract of chayote fruit 150 mg / kgBB, p.o.
h. group 8, the treatment group that was induced by Streptozotocin 50 mg / kg + nicotinamide (120 mg / kg) + HFD, with the ethyl acetate fraction of chayote 50 mg / kg, p.o.
i. group 9, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with the ethyl acetate fraction of chayote 100 mg / kgBB, p.o.
j. group 10, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with the ethyl acetate fraction of chayote 150 mg / kg, p.o.
k. group 11, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with the n fraction of chayote's hexane 50 mg / kgBB, p.o.
l. group 12, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with fraction n hexane of chayote fruit 100 mg / kgBW, p.o.
m. group 13, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with n hexane fraction of chayote fruit 150 mg / kg, p.o.
n. group 14, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with chayote juice 50 mg / KgBW p.o
o. group 15, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with chayote juice 100 mg / KgBW p.o
p. group 16, the treatment group that was induced by Streptozotocin 50 mg / kgBW + nicotinamide (120 mg / kg) + HFD, with chayote juice 150 mg / KgBW p.o
q. group 17, the treatment group that was induced by Streptozotocin 50 mg / kg + nicotinamide (120 mg / kg) + HFD, with metformin 500 mg / KgBW p.o
r. group 18, the treatment group that was induced by Streptozotocin 50 mg / kg + nicotinamide (120 mg / kg) + HFD, with simvastatin 500 mg / KgBW p.o

DISCUSSION

Hyperlipidemia is a common metabolic disorder that causes cardiovascular disease, where there is an increase in the concentration of fat or lipo protein which results in impaired fat metabolism. This is based on high carbohydrate intake, familial hypercholesterolemia (FH), obesity, and diabetes (Yao et al., 2020). In this study, it was shown that the chayote extracts 150 mg/ kgBW per oral was better at increasing HDL levels compared to the ethyl acetate fraction, n hexane fraction and juice. This is because the ethanol solvent is able to attract bioactive compounds in the extract, both polar and non-polar (Saleh, 2016), while the n-hexane solvent is non-polar and ethyl acetate is semipolar so that a more specific fraction attracts bioactive compounds according to the polarity of the solvent (Da'i et al., 2020). Chayote extract using ethanol solvent contains alkaloids, flavonoids, glycosides, sapaonins, tannins and triperten (Siahaan, 2020). This study is in line with Neeraja et al. (2015), that the ethanol extract 200 mg/KgBW can significantly increase HDL.

Bioactive flavonoid compounds can reduce cholesterol levels through cholesterol synthetase inhibition, LDL receptor expression, cholesterol acyltransferase-1 (ACAT-1), cholesterol acyltransferase-2 (ACAT-2), MTP (microsomal triglyceride transfer protein). In addition, flavonoids work as antiatherogenic by inhibiting hepatic acyl CoA: cholesterol acyltransferase (ACAT), reducing cholesterol absorption and the expression of VCAM-1 (vascular cell

adhesion molecule-1) and MCP-1 (monocyte chemoattractant protein-1) which plays an important role in adhesion. monocytes in the endothelium of blood vessels (Zeka et al., 2017).

Tannin bioactive compounds can reduce lipid metabolism by inhibiting lipase performance thereby reducing muscle fat accumulation (Yao et al., 2019). Tannins also affect fatty acid catabolism in the liver by controlling lipoprotein hydrolysis and fat absorption (Ravichandiran et al., 2012). In HepG2 cells, tannins inhibit the accumulation of TG and cholesterol (Oh et al., 2018)

Saponin bioactive compounds have an effect in inhibiting pancreatic lipase, controlling body weight by inhibiting adipogenesis, controlling appetite (Marrelli et al., 2016). In broilers, sapaonin has the effect of inhibiting the expression of HMG-CoA reductase mRNA in the liver, accelerating the excretion of bile acids through feces and reducing hepatic cholesterol synthesis (Liu et al, 2016).

Alkaloid bioactive compounds also have a role in the activation of the enzyme lecithin cholesterol acyltransferase (LCAT) which inhibits cholesterol biosynthesis and plays an important role in the cholesterol transfer pathway when cells are unable to metabolize cholesterol. With the LCAT enzyme, HDL works more effectively to stimulate the flow of cholesterol from cells to receptors in the liver (Said et al, 2018).

From the results of this study it can be concluded that the ethanol extract 150 mg / kgBW per oral is better to increase HDL, because ethanol solvent contains more complex bioactive compounds.

AUTHOR CONTRIBUTION

Jekson Martiar Siahaan, Endy Julianto and Tengku Muhammad Fauzi are those who carry out sample preparation, spectrophotometric examination, data interpretation and article preparation.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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