

The Effect of Chayote Juice (*Sechium Edule*) on Mda and Il-6 Levels (Experimental Study on Male Wistar Rats Induced with High-Fat Diet)



Ayu Chasmirahayu¹, Joko Wahyu Wibowo², Titiek Sumarawati³

¹Postgraduate student of Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung, Jl Kaligawe KM 4 Semarang 50012

^{2,3}Department of Biomedical Sciences, Faculty of Medicine, Universitas Islam Sultan Agung, Jl Kaligawe KM 4 Semarang 50012

ABSTRACT: Dyslipidemia is an increase in total cholesterol, Low-Density Lipoprotein (LDL), triglycerides, and a decrease high-Density Lipoprotein (HDL), Consequences of consuming fat cause the metabolism of free fatty acids resulting in an imbalance between free radicals and the body's natural antioxidants which causes a condition of oxidative stress. Oxidative stress results in tissue damage which triggers an inflammatory reaction that releases pro-inflammatory cytokines such as Interleukin-6 (IL-6) and triggers Malondialdehyde (MDA) due to lipid oxidation in tissues. Consuming antioxidants from outside the body can neutralize this condition, such as chayote juice. The aim of this study is to know the effect of giving chayote juice on the rate of MDA and IL-6 in male Wistar rats who are given a high-fat diet. The research method is experimental research with a post-test-only control group design. The study subjects were 24 male Wistar rats, randomly divided into 4 groups. Group K1 was given standard feed and distillate water. Group K2 was without chayote juice but was given a high-fat diet. Groups- K3 and K4 were given a high-fat diet and chayote juice at doses of 1.8mL/200gBW/day and 3.6mL/200gBW/day, respectively. The study was conducted at IBL FK UNISSULA for 29 days by taking blood to check MDA levels using the TBARS and IL-6 methods using the ELISA method. Results showed that the lowest average MDA level was in the K4 group (0.058 ng/L) and the lowest average IL-6 level was in the K3 group (4.513 ppm). One-way ANOVA test result showed a significant difference in MDA levels with $p = 0.021$ and IL-6 levels showed no significant difference with $p = 0.108$. The Tahmane test result showed the MDA levels in K1 and K4 showed a significant difference in K2 ($p < 0.05$). Test LSD test result showed the IL-6 levels in K3 showed a significant difference to K2 ($p < 0.05$). The conclusion of this study was the administration of chayote juice significantly reduced levels of MDA and IL-6 in the group of rats that received a high-fat diet.

KEYWORDS: Siam pumpkin juice, MDA, IL-6

I. INTRODUCTION

Dyslipidemia is an increase in total cholesterol, Low-Density Lipoprotein (LDL), triglycerides, and a decrease High-Density Lipoprotein (HDL) in blood plasma. Dyslipidemia is a risk factor for cardiovascular disease.¹ Cardiovascular disease due to dyslipidemia occurs due to oxidative stress, LDL oxidation, and changes in inflammatory status.^{2,3} Increased LDL due to consumption of fat causes free fatty acid metabolism resulting in an imbalance between free radicals and the body's natural antioxidants which causes a condition of oxidative stress. Oxidative stress causes damage to the vascular endothelium which triggers an inflammatory reaction.⁴ Society chooses natural therapy to control hyperlipidemia,⁵ one of the ways used is with plants that have natural antioxidants such as chayote juice (*Sechium edule*).⁶

A global Burden of Disease Study reported that nearly 17.6 million deaths were caused by Cardiovascular Disease (CVD).⁷ Cardiovascular disease accounts for the highest mortality in the world where around 80% of the global death rate comes from developing countries.⁸ Cardiovascular disease is the main cause of death in Southeast Asia.^{9,10} The prevalence of cardiovascular disease in Indonesia in 2013 was 0.5% or 883,447 people, meanwhile, in 2018, this figure increased to 1.5% or around 1,017,290 people.^{11,12} Previous studies have shown that effective management of patients with dyslipidemia reduces the incidence, mortality, and disease burden of Cardiovascular Disease (CVD).⁷

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Chayote juice (*Sechium edule*) is an herbal plant that contains natural antioxidant compounds such as flavonoids, polyphenols, carotenoids, vitamin C, and vitamin E. These natural antioxidants have the benefit of protecting the body against cell damage caused by ROS, being able to lower lipid profiles.¹³ Dyslipidemia causes oxidative stress as a result of increased cholesterol accumulation triggering the production of reactive oxygen species (ROS) so that antioxidants in the body are reduced.¹⁴ An increase in ROS that exceeds the capacity of antioxidant enzymes in the body will cause an increase in lipid peroxidation which damages proteins, DNA (Deoxy Nucleic Acid), and the cell membranes of the body.¹⁵

A high-fat diet causes an increase in plasma lipopolysaccharide (LPS) and activates toll-like receptor 4 (TLR4) resulting in increased levels of pro-inflammatory cytokines such as interleukin-6 (IL-6).¹⁶ Siamese pumpkin can prevent oxidative stress because it can act as an antioxidant, which works directly with the flavonoid content to prevent oxidative stress, thereby reducing tissue damage, reducing oxidative damage, lipid peroxidation, and inflammation.^{17,18} Based on the description above, a study was conducted on the effect of giving chayote juice (*Sechium edule*) against the MDA rate and interleukin-6 in mice fed a high-fat diet.

II. MATERIAL AND METHOD

Experimental Subjects

The research subject is male Wistar rats which were divided into four groups, the control group (K1), the control group which was given a high-fat diet (K2), the treatment group which was given chayote juice therapy at a dose of 1.8 mL/200gBB/day (K3), and the treatment group which was given chayote juice therapy at a dose of 3.6 mL/200 g BW/day (K4). The chayote used in this study was peeled and then washed and then juiced.

Administration of Chayote Juice

The K4 group was given the chayote juice dose of 3.6mL/200gBW/day and a high-fat diet. The K3 group by giving a chayote juice dose of 1.8mL/200gBW/day and a high-fat diet, then the control group (K1) by giving a standard-feeding and distilled water. The control group (K2) which was given a high-fat diet and distilled water

Data Analysis

The normality and homogeneity data test using Shapiro Wilk and Levene test. The data of MDA and IL-6 levels were analyzed using the One-Way ANOVA, the Tamhane, and the LSD test.

III. RESULT

The Effect of Chayote Juice on MDA Levels

Table 1 shows that the lowest mean MDA level was in the treatment group (K4) with the administration of a chayote juice dose of 3.6mL/200gBW/day and a high-fat diet, then followed by the treatment group (K3) by giving chayote juice dose of 1.8mL/200gBW/day and a high-fat diet, then the control group (K1) by standard-standard and distilled water. The control group (K2) which was given a high-fat diet and distilled water obtained the highest average MDA level. All groups of MDA levels based on the Shapiro Wilk test show a normal distribution with a p-value <0.05 and homogeneity test using Levene test the results are not homogeneous with a p-value of 0.001 (p <0.05) then data analysis using a parametric test One-Way ANOVA. One-Way ANOVA test results showed significant differences in all groups with a p-value of 0.021 (p <0.05).

Table 1. Results of Average Analysis, Normality Test, Homogeneity Test on MDA Levels and IL-6 Levels

b	Group				Sig.(p)
	K1 N=6	K2 N=6	K3 N=6	K4 N=6	
MDA (ppm)					
Mean	0.072	0.096	0.065	0.058	
Std. deviation	0.011	0.003	0.033	0.020	
Shapiro Wilk	0.073*	0.050*	0.644*	0.627*	
Levene Test					0.001
One Way Anova					0.021***
IL-6 (ng/L)					
Mean	5.043	5.760	4.513	4.812	
Std. deviation	0.985	0.543	0.966	0.861	
Shapiro Wilk	0.154*	0.993*	0.612*	0.118*	
Levene Test					0.334**
One Way Anova					0.108

Information: *Normal p>0.05 **Homogeneous p>0.05 ***Significant p<0.05

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Table 2. Differences in MDA levels between the 2 groups using the test LSD

Group	<i>p-Value</i>
K1 vs K2	0.012*
K1 vs K3	0.998
K1 vs K4	0.649
K2 vs K3	0.360
K2 vs K4	0.029*
K3 vs K4	0.998

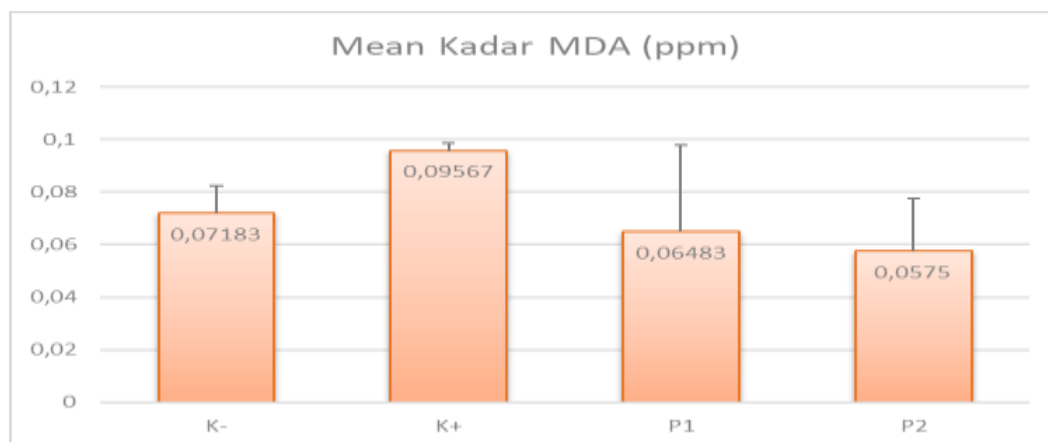


Figure 1. The average of MDA levels between groups

Based on the data above (Figure 1 and Table 2), it shows that the MDA level in group (K1) has a significant difference in group (K2) with a *p*-value of 0.012 ($p < 0.05$) while there is no significant difference in group (K3) with a *p*-value of 0.998 and group (K4) with a *p*-value of 0.649 ($p > 0.05$). Group (K1) did not have a significant difference to group (K3) with a *p*-value of 0.360 ($p > 0.05$) but there was a significant difference to group (K4) with a *p*-value of 0.029 ($p < 0.05$). There was no significant difference between group (K3) and group (K4) with a *p*-value of 0.998 ($p > 0.05$). Based on the data above, it can be concluded that administration of chayote juice at doses of 1.8mL/200gBW/day and 3.6mL/200gBW/day has a significant effect on decreasing MDA levels in male Wistar rats given a high-fat diet so that the hypothesis statement is accepted.

The Effect of Siamese Pumpkin Juice on IL-6 Levels

The lowest mean IL-6 levels are in Table 1, namely in the treatment group (K3) with the administration of chayote juice at a dose of 1.8 mL/200gBB/day with a high-fat diet, then successively followed by the treatment group (K4) with the administration of chayote juice dose of 3.6mL/200gBB/day with a high-fat diet and the control group (K1) with standard feeding and distillate water. The control group (K2) which was given a high-fat diet and distilled water had the highest average IL-6 level. All groups of IL-6 levels based on the Shapiro Wilk *test* showed a normal distribution with a value of $p > 0.05$ and homogeneity test using Levene test the results are homogeneous with a value of $p = 0.334$ ($p > 0.05$) then the data analysis uses a parametric test using One-Way ANOVA. One-Way ANOVA test result showed no significant difference in all groups with a *p*-value of 0.108 ($p > 0.05$).

Table 3. Differences in IL-6 levels between the 2 groups using the test LSD

Group	<i>p-Value</i>
K1 vs K2	0.163
K1 vs K3	0.297
K1 vs K4	0.645
K2 vs K3	0.020*
K2 vs K4	0.070
K3 vs K4	0.554

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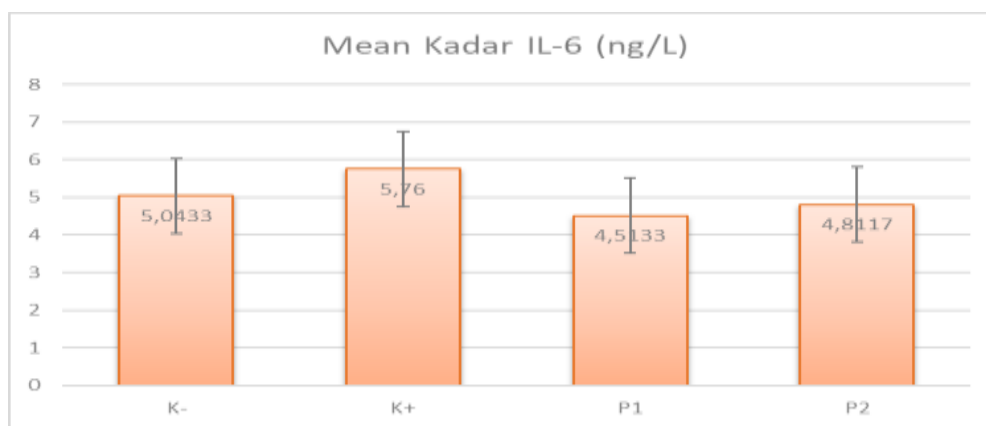


Figure 2. The average of IL-6 levels between groups

Based on the data above (Figure 2 and Table 3). it showed IL-6 levels in group (K1) there was no significant difference to group (K2) with a p-value of 0.163, group (K3) with a p-value of 0.297 and group (K4) with a p-value of 0.645 ($p > 0.05$). Group (K2) had a significant difference to group (K3) with a p-value of 0.020 ($p < 0.05$) but there was no significant difference to group (K4) with a p-value of 0.070 ($p > 0.05$). There was no significant difference between group (K3) and group (K4) with a p-value of 0.554 ($p < 0.05$). Based on the data above, it can be concluded that giving chayote juice with a dose 1,8mL/200gBB/day and 3,6mL/200gBB/day had a significant effect on decreasing IL-6 levels in male Wistar rats given a high-fat diet so that the hypothesis statement is accepted.

IV. DISCUSSION

High-fat intake can lead to the accumulation of adipocytes which induce dyslipidemia. This high intake can also increase cholesterol esters, especially LDL, triglycerides, and levels of reactive oxygen species (ROS).¹⁹ An imbalance between energy intake and energy used in physical activity will increase fat tissue deposits, resulting in obesity and accumulation of visceral fat.²⁰ This condition causes oxidative stress and affects body changes.¹⁸ The treatment group showed increased cholesterol levels (> 54 mg/dL), LDL (> 27.2 mg/dL), and HDL (< 35 mg/dL) as a result of being given a high-fat diet using egg yolks of 2 ml/head/day by means of in sonde for 14 days in (K2), (K3), and (K4).

The results of examining MDA levels in the control group (K2) who were given a high-fat diet without giving squash juice experienced a significant increase compared to the control group (K1), the group that was given chayote juice at a dose of 1.8 mL/200 gBW/day (K3) and 3.6 mL/200 gBW/day (K4) as shown in Table 1. This suggests that hypercholesterolemia will trigger lipid peroxidation. Lipid peroxidation is a reaction that occurs between free radicals and polyunsaturated fatty acids (*polyunsaturated fatty acid*, PUFA) which are present in cell membranes and LDL. As a result, the blood vessels can become thicker, forming products that are toxic to the body, Malondialdehyde (MDA).²¹ MDA levels in the group given a high-fat diet and administration of chayote juice at doses of 1.8 mL/200 gBW/day and 3.6 mL/200 gBW/day decreased as shown in Table 1. Siamese pumpkin contains active compounds of flavonoids, polyphenols, vitamin C, vitamin E, and carotenoids. Flavonoids in chayote with 3 c-glycosides and 5 o-glycosides can reduce total cholesterol by inhibiting the absorption of cholesterol in the intestine. Polyphenols as antioxidants donate -OCH₃ and -OH groups which can turn free radicals into stable compounds.²¹

The results of examining IL-6 levels in group (K2) which was given a high-fat diet without giving squash juice experienced a significant increase compared to group (K1), the group that was given chayote juice at a dose of 1.8 mL/200 gBW/day (K3) and 3.6 mL/200 gBW/day (K4) as shown in Table 1. Feeding fat can induce ROS which will have an impact on lipid metabolism. When there is a disturbance of lipid metabolism, there will be an increase in adipose tissue mass caused by the incoming energy being higher than the energy expended, resulting in an increase in the size and number of adipose tissue. An increase in the size and number of adipose tissue leads to the production of pro-inflammatory cytokines, one of which is IL-6. This is caused by oxidative stress which will activate Bax in mitochondria so that release occurs cytochrome-c.²² This release has an impact on inhibiting the flow of electrons in the respiratory chain. Levels β -oxidation and FFA also increased so that there was an increase in the levels of NADH, FADH, and sending electrons to the respiratory chain. This imbalance in sending electrons and removing electrons causes an accumulation of electrons in the respiratory chain which will form an excess nitric oxide (NO) by nitric oxide synthase (iNOS) which then activates NF- κ B expression to induce IL-6.²³

IL-6 levels in the group given a high-fat diet and administration of chayote juice at doses of 1.8 mL/200gBW/day and 3.6 mL/200gBW/day decreased as shown in Table 1. Siamese pumpkin has benefits as an antibacterial, antioxidant, and anti-

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inflammatory depending on the bioactive compounds contained in it. The COX-2 enzyme is an enzyme involved in the production of prostaglandins and inflammatory cytokines such as IL-6, the flavonoids in chayote can help suppress the activity of the COX-2 enzyme so that the production of prostaglandins and IL-6 can be suppressed. This can help lower IL-6 levels in the body. Then the flavonoid compounds in chayote can help inhibit NF-κB activation so that IL-6 production can be suppressed. It can also help lower IL-6 levels in the body.²⁴ The limitation of this study was the stability of the body weight of the rats before and after treatment, this was due to the administration of doses that did not match the body weight of the rats. Rats with an average body weight of 250 grams should be given a dose according to body weight so it is hoped that research can be carried out using a dose of chayote juice according to the rat's body weight. Researchers did not carry out total cholesterol examinations after the treatment of the rats so it is expected that total cholesterol examinations could be carried out after the treatment.

V. CONCLUSION

The administration of chayote juice at a dose of 1.8 mL/200 gBW/day and 3.6 mL/200gBW/day can decrease the MDA and IL-6 levels in male Wistar rats given a high-fat diet.

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