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EFFECT OF GARLIC EXTRACT (ALLIUM SATIVUM) ON DYSLIPIDEMIA IN MALE WISTAR RATS WITH A DIET HIGH IN FAT AND PTU.

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ABSTRACT

Dyslipidemia is a disorder of lipid metabolism that can increase the risk of cardiovascular disease. This disorder is often caused by a diet high in fat and the use of chemical compounds such as propylthiouracil (PTU). This study aims to explore the potential of garlic methanol extract (Allium sativum) in overcoming dyslipidemia as an alternative therapy, with minimal effect compared to conventional drugs. This experimental study used male Wistar mice divided into six treatment groups with different doses of garlic extract and simvastatin as positive controls. Treatment was carried out for four weeks after induction of dyslipidemia, with a diet high in fat and PTU. The blood lipid profile of mice was measured for total Cholesterol, LDL, HDL, and triglyceride levels, as well as SGOT and SGPT levels, to evaluate potential hepatotoxicity. The results showed that garlic methanol extract may affect blood lipid profiles, with lower increases in total Cholesterol, triglycerides, and LDL in the treatment group with a dose of garlic extract compared to the control group. However, the effect of the extract on HDL levels is quite significant, and higher doses tend to increase SGOT and SGPT levels, suggesting an effect on liver function. This study shows that garlic extract has potential as an alternative therapy for dyslipidemia, but further attention is needed regarding the impact of hepatotoxicity at high doses.

Keywords: Dyslipidemia, garlic methanol extract, lipid profile, SGOT, SGPT, alternative therapies

INTRODUCTION

Dyslipidemia is a lipid metabolism disorder that can increase the risk of cardiovascular disease and is characterized by an imbalance in Cholesterol, LDL, triglycerides, and HDL levels in the blood (Lin et al., 2018). A high-fat diet and the use of compounds such as propylthiouracil (PTU) can trigger this disorder, making it essential to carry out the prevention and treatment of dyslipidemia (Go et al., 2014). Some types of dyslipidemia associated with atherogenic lipid accumulation can increase the risk of cardiovascular disease (Erwinanto et al., 2013; Arsana et al., 2015). Medications such as statins, fibrates, niacin, and ezetimibe are often used to lower blood lipid levels. However, these medications can cause side effects such as muscle pain, indigestion, and an increased risk of type 2 diabetes (Purva et al., 2020; Saragih, 2020). In Indonesia, the prevalence of dyslipidemia, with 35.9% of the population having abnormal cholesterol levels, especially in urban areas (Health Research and Development Agency of the Ministry of Health of the Republic of Indonesia, 2013). Herbal plants, such as Garlic (Allium sativum), have phytochemical compounds that can help treat dyslipidemia with minimal side effects compared to conventional drugs (Anneke & Sulistiyaningsih, 2018). Garlic contains compounds such as phenols, flavonoids, and saponins, which have anti-inflammatory, antioxidant, and antibacterial effects (Saragih & Arsita, 2019; Yanti et al., 2011). This study aims to explore the potential of garlic extract in overcoming dyslipidemia as an alternative therapy.

RESEARCH METHODS

This study is an experimental research with a Pre-test and Post-test group control design that uses male Wistar mice as the research object. The study was conducted over six weeks, with the first week for manufacturing garlic methanol extract, a second week for acclimating rats, and the remaining four weeks for treating rats. The experimental animal used was a male Wistar rat with a body weight of 180-200 grams and 2-4 months old. Samples were calculated based on Federer's formula with a minimum of 4 mice for each treatment group.
The study variables consisted of independent variables, namely the dose of garlic methanol extract; the bound variable, namely the lipid profile of rat blood serum; and control variables, namely body weight and total cholesterol levels before treatment. This research uses analytical scales, UV spectrophotometers, microscopes, and other laboratory equipment. The ingredients used include Garlic (Allium sativum), methanol, Na-CMC, simvastatin, and phytochemical screening reagents.

The research began with determining garlic samples obtained from traditional markets, identified at the Herbarium Medanense FMIPA USU, and then made simplistic. The simplicia are extracted with methanol solvent using maceration techniques. The extracts obtained are phytochemically tested to identify the content of phenols, steroids, terpenoids, saponins, flavonoids, tannins, and alkaloids. Furthermore, the anti-dyslipidemia effect was tested by giving mice a diet high in fat and PTU to induce dyslipidemia. The mice were divided into six treatment groups with different doses of garlic extract and simvastatin as positive controls.

Lipid profile measurements were done by taking blood samples from rat hearts, then centrifugating and analyzing for total Cholesterol, LDL, HDL, and triglyceride levels using colorimetric methods. In addition, SGOT and SGPT levels were also measured with the Dyasis® reagent kit to determine potential hepatotoxicity. The data obtained were analyzed using SPSS 25, with the One-Way ANOVA test for normal data and the Kruskal-Wallis test for abnormal data, to see significant differences between treatment groups.

RESEARCH RESULTS

The sample of Garlic (Allium sativum) used in this study was obtained from one of the traditional markets in Medan City. The sample was identified at the Medanesea Herbarium of the Faculty of Mathematics and Natural Sciences, University of North Sumatra, and the results of its identification showed that the plant had the scientific name Zanthoxylum acanthopodium, which belongs to the Rutaceae family. After extraction using the maceration method, Garlic methanol extract was obtained with the following characteristics: the weight of fresh simplicia used in the extraction process was 820 grams, which after drying produced dry simplicia powder weighing 215 grams. The extraction was carried out using 2100 mL of methanol solvent. After the evaporation process, the resulting extract had a final weight of 15.10 grams, with a yield of 7.03%, which shows the efficiency of the extraction method. Phytochemical screening showed that garlic methanol extract contained several phytochemical compounds, such as alkaloids, flavonoids, tannins, steroids, and terpenoids. However, some tests did not show positive results for specific compounds. Data normality analysis was carried out on several parameters, including body weight, total Cholesterol, lipid profile, and SGOT and SGPT levels to evaluate the anti-dyslipidemia. The normality test results showed that some parameters, such as weight, total Cholesterol after treatment, and LDL levels, were usually distributed. In contrast, other parameters, such as total Cholesterol before induction, triglycerides, and SGOT levels, were not normally distributed. In terms of weight, no significant differences were found between treatment groups with a p> value of 0.05, suggesting that prior to treatment, the weight of the mice in this study was balanced, and there was no initial bias in weight distribution between groups. Based on these data, it can be concluded that the characteristics of the extract and the phytochemical screening results of Garlic provide an initial idea of the potential of this plant in addressing dyslipidemia. However, the data distribution for some parameters shows variations that require further attention in subsequent statistical analysis.

Table 1 Comparison of Total Cholesterol Before and After Dietary High-Fat Diet in All Treatment Groups

Treatment Groups	Total Cholesterol (mg/dL)	
	Before Induction	**After Induction**
Usual	114.80 (109-117)	118.30 (116-121)b
Standard	111.20 (99-114)	210.40 (204-214)a
Control	115.90 (109-116)	212.10 (209-214)b
Garlic Methanol Extract (Allium sativum)-I	114.70 (108-118)	211.80 (208-213)b
Garlic Methanol Extract (Allium sativum)-II	109.80 (98-113)	209.90 (208-211)b
Garlic Methanol Extract (Allium sativum)-III	115.20 (115-118)	210.75 (208-211)B
P value	**0.859**	**0.003**

The data is displayed as Median (Range). The P value was obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences.

Table 1 shows the comparison of total Cholesterol before and after the administration of a high-fat diet in all treatment groups. The "Normal" group had an increase in Cholesterol from 114.80 mg/dL to 118.30 mg/dL ($p < 0.05$). The "Standard" and "Control" groups showed significant improvements, with total Cholesterol increasing from 111.20 mg/dL to 210.40 mg/dL ($p = 0.003$) and from 115.90 mg/dL to 212.10 mg/dL ($p = 0.003$), respectively. The group given methanol extract of Garlic (Allium sativum) also experienced an increase in Cholesterol, although it was not statistically significant. Overall, a diet high in fat and Garlic extract increases cholesterol levels.

Table 2 Comparison of Lipid Profiles in All Rats Treatment Group

Treatment Groups	Total Cholesterol (mg/dL)	Triglycerides (mg/dL)	LDL (mg/dL)	HDL (mg/dL)

Normal	162.75 ± 2.15a	98.80 (96-99)a	59.90 ± 1.55a	65.50 (60-63)a
Standard	143.00 ± 0.70b	104.50 (100-104)b	62.50 ± 1.10b	60.80 (59-64)a
Control	178.80 ± 5.50c	169.80 (167-178)c	111.50 ± 6.20c	28.40 (67-45)b
MBA-I Extract	167.10 ± 1.40d	165.00 (163-164)d	85.20 ± 2.40d	56.20 (55-58)b
MBA-II Extract	162.90 ± 2.10e	119.50 (112-121)e	76.40 ± 1.10e	60.10 (59-62)a
MBA-III Extract	150.50 ± 1.00e	109.20 (107-111)f	67.90 ± 1.20f	60.80 (59-62)a
P value	< 0.05	0.013	< 0.05	0.00

*Data is displayed as Mean ± SD. The P value was obtained from the One Way ANOVA analysis; **Data is displayed as Median (Range). The P value was obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences

Table 2 compares lipid profiles across the entire treatment group of mice, including total Cholesterol, triglycerides, LDL, and HDL. The control group had the highest total cholesterol (178.80 ± 5.50 mg/dL), followed by the MBA-I (167.10 ± 1.40 mg/dL) and normal (162.75 ± 2.15 mg/dL) extract groups. MBA-III extract had the lowest total Cholesterol (150.50 ± 1.00 mg/dL) with significant differences ($p < 0.05$). In triglycerides, the control group recorded the highest value (169.80 mg/dL), while the normal group had the lowest value (98.80 mg/dL), with significant differences ($p = 0.013$). The control group also had the highest LDL levels (111.50 ± 6.20 mg/dL), while the MBA-I and MBA-II extract groups had lower LDL levels (85.20 ± 2.40 mg/dL and 76.40 ± 1.10 mg/dL). A p-value smaller than 0.05 indicates a significant difference. For HDL, the control group had the lowest levels (28.40 mg/dL). In contrast, the normal and extracted groups of MBA-II and MBA-III showed higher HDL levels (about 60 mg/dL), with very significant differences ($p = 0.00$). Overall, MBA extract affects the lipid profile of mice, with effects varying based on dosage and treatment.

Table 3 Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Groups	Up to SGOT (U/L)	Up to SGPT (U/L)
Usual	23.50 (22-29) a	43.20 ± 1.10 A
Standard	105.20 (101-110) b	168.50 ± 1.50 b
Control	138.60 (135-145) c	94.30 ± 1.10 c
Extract MBA-I 100 mg/kgBB	110.30 (107-113) d	98.40 ± 3.20 p
MBA-II Extract 150 mg/kgBB	123.70 (119-124) e	111.10 ± 4.10 e
MBA-III Extract 200 mg/kgBB	129.50 (125-131) f	138.20 ± 2.50 b
P value	**0.002**	**< 0.05**

*Data is displayed as Mean ± SD. The P value was obtained from the One Way ANOVA analysis; **Data is displayed as Median (Range). The P value was obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences

Table 3 compares SGOT and SGPT levels across treatment groups with different doses of garlic methanol extract. The Normal group had the lowest levels of SGOT and SGPT, 23.50 (22-29) U/L and 43.20 ± 1.10 U/L, respectively. The Standard group (without extract treatment) showed higher levels of SGOT and SGPT, namely 105.20 (101-110) U/L and 168.50 ± 1.50 U/L. The Control group also showed increased levels of SGOT and SGPT, with values of 138.60 (135-145) U/L and 94.30 ± 1.10 U/L. The group given garlic methanol extract with different doses showed increased SGOT levels and SGPT along with the increase in dose. The MBA-I Extract Group (100 mg/kgBB) had SGOT levels of 110.30 (107-113) U/L and SGPT 98.40 ± 3.20 U/L. MBA-II Extract Group (150 mg/kgBB) showed SGOT levels of 123.70 (119-124) U/L and SGPT 111.10 ± 4.10 U/L, while MBA-III Extract (200 mg/kgBB) had the highest SGOT levels, which were 129.50 (125-131) U/L and SGPT 138.20 ± 2.50 U/L. P values showed significant differences in SGOT ($P = 0.002$) and SGPT ($P < 0.05$) levels between treatment groups, which showed that the dose of garlic methanol extract affected liver enzyme levels, with a more pronounced effect at higher doses. Garlic (Allium sativum) is often known as a culinary ingredient and a traditional medicinal plant. Still, in this study, the plant used was Zanthoxylum acanthopodium, which comes from the Rutaceae family, not Allium sativum. This plant, better known by the local name "andaliman," is widely used in typical Sumatran cuisine and traditional medicine to enhance the nutty taste and aid digestion.

DISCUSSION

The characteristics of the Garlic (Allium sativum) methanol extract obtained through the extraction process can be seen in the following data: 820 grams of fresh simplicia are used for the extraction process, producing 215 grams of dried simplicia powder after drying. Extraction was carried out using a methanol solvent of 2100 mL, and after the evaporation process, the resulting extract had a final weight of 15.10 grams. The yield obtained is 7.03%, reflecting the extraction process's efficiency. This yield can be influenced by factors such as the amount of active compounds in the raw material or extraction conditions such as temperature and time. Nonetheless, extraction with methanol solvents is generally effective in extracting active compounds from plants, including antioxidant, antibacterial, and other compounds found in Garlic (Allium sativum) (Zhou et al., 2019).

Concerning total cholesterol parameters, the control group showed the highest cholesterol levels (178.80 ± 5.50 mg/dL). The groups given MBA-I (100 mg/kgBB) and MBA-III (200 mg/kgBB) extracts showed a decrease in cholesterol levels, especially in the MBA-III group (150.50 ± 1.00 mg/dL), which may be due to the hypocholesterolemic effects of the active compounds in Garlic, such as allicin and other sulfur compounds, which have been proven in previous studies (Ried et al., 2016). In triglycerides, the control group recorded the highest values (169.80 mg/dL). In comparison, the MBA-III group showed lower levels (109.20 mg/dL), indicating the potential of garlic extract to lower triglycerides, according to existing research (Sengupta et al., 2018). The control group showed the highest levels of LDL (111.50 ± 6.20 mg/dL), which is at risk for cardiovascular disease. The groups given MBA-I and MBA-II extracts showed decreased LDL levels, potentially improving lipid profiles. Garlic compounds function as antioxidants that reduce LDL oxidation, reducing the risk of atherosclerosis (Basu et al., 2016). In HDL, the control group had low HDL levels (28.40 mg/dL), which increased the risk of heart disease. In contrast, the normal group and extracts of MBA-II and MBA-III showed higher HDL levels (about 60 mg/dL), which signaled protection against heart disease (Sacks et al., 2016).

Levels of SGOT and SGPT, indicators of liver damage, increased in the control group, indicating potential liver damage due to external factors (Mansouri et al., 2018). The group given MBA extract showed increased liver enzyme levels with dose, with MBA-III (200 mg/kgBB) being the highest. Although high doses of garlic extract have a positive effect on liver health, they can temporarily increase liver enzymes (Liu et al., 2018). Previous research has shown that high doses can increase liver enzymes before providing long-term therapeutic effects (Gholami et al., 2019).

At low to moderate doses, garlic extract protects the liver through antioxidant and anti-inflammatory mechanisms (Salehi et al., 2020). The pro-oxidant effects at high doses can temporarily increase liver enzymes, which then show therapeutic effects. This study's results confirm that the extract's dose affects liver enzyme levels and lipid profile, with high doses having a greater impact, although long-term effects take time. Further research is needed to understand the long-term implications of garlic methanol extract.

CONCLUSION

This study revealed that methanol extract from Zanthoxylum acanthopodium (andaliman) can lower Cholesterol, triglycerides, and LDL and increase HDL, which supports heart health. However, high doses increase liver enzyme levels (SGOT and SGPT), which indicates changes in liver metabolism due to pro-oxidant effects. Although these extracts have positive potential, more research is needed to understand the long-term impact, optimal dosage, and underlying mechanisms, as well as involving a variety of test animal models and more diverse populations.

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