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Anti-Dislipidemia Effectiveness Test of Turmeric Ethanol Extract (Curcuma Longa) in Male Wistar Mice Given Propylthiouracil (PTU)

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Abstract: *Dyslipidemia is a lipid metabolic disorder that is a risk factor for coronary heart disease (CHD). According to the American Heart Association, data from 2013 to 2016, as many as 92.8 million adults in America have total cholesterol of more than 200 mg / dL. Curcumin, the main compound in turmeric, can lower cholesterol levels due to inhibiting the reabsorption of cholesterol derived from the outside (exogenous) and increasing the enzyme HMG-CoA reductase inhibitor so that fat synthesis can run well. The purpose of this study was to find out the effectiveness of mangosteen peel ethanol extract as an anti-dyslipidemia in male Wistar rats given Propylthiouracil (PTU). This study is an experimental study with a Pre-test and Post-test group only control design approach that uses male Wistar rats as test animals and turmeric extract. The study was conducted in March 2021, at the Herbarium Medanese FMIPA USU, the Pharmacognosy Laboratory of the FACULTY of Pharmacy USU, and the Laboratory of Pharmaceutical Pharmacology USU. Descriptive data analysis (Central tendency and Dyspersi) in the form of lipid profiles (LDL, HDL, Total Cholesterol, and Triglycerides), color, texture, weights. Then analyzed with One-Way Anova if the distributed data is normal, if the distributed data is not normal, then the Kruskal-Wallis test is used. The results and conclusions, turmeric ethanol extract (Curcuma Longa) III (151.70 ± 0.95 mg/dl) can significantly decrease total cholesterol compared to the control group (178.50 ± 6.05mg/dl) (P-value < 0.05). Turmeric ethanol extract (Curcuma Longa) III (110.00 ± (109-112) mg/dl) may significantly lower triglyceride levels compared to the control group (167.00 (162-179) mg/dl). (Value P = 0.027). Turmeric ethanol extract (Curcuma Longa) III (68.50 ± 1.28 mg/dl) significantly lowered LDL levels compared to the control group (107.20 ± 3.60 mg/dl). (P-value < 0.05). Turmeric ethanol extract (Curcuma Longa) III, (61.00 (60-62) mg/dl) may significantly increase HDL levels compared to the control group (28.50 (37-45) mg/dl). (Value P = 0.027). Turmeric ethanol extract (Curcuma Longa) III significantly lowered SGOT (Value = 0.027) and SGPT (Value P < 0.05) compared to the control group.*
Keywords: *curcuma longa; dyslipedemia; propylthiouracil*

I. Introduction

Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in lipid fraction in plasma and is a risk factor for various diseases that are still a major problem in Indonesia such as coronary heart disease (CHD) (Irmadoly et al., 2014). The main lipid fraction abnormalities are the increase in total cholesterol levels, LDL cholesterol (Low Density Lipoprotein), triglycerides, and decreased HDL (High Density Lipoprotein) cholesterol(Dipiro J et al., 2015); (Ardhani et al., 2017). The disease is also one of the risk factors for atherosclerosis that can cause coronary heart disease (CHD) (D'Agostino et al., 2008).

According to American Heart Association data from 2013 to 2016, 92.8 million people or 38.2% of adults in the United States have total cholesterol over 200 mg/dl(Aparicio et al., 2021). Cardiovascular disease is the most common non-communicable disease in the world and was the cause of 17.8 million deaths in 2017 (Wulansari, 2020). The number of heart disease sufferers in Indonesia reached 1,017 million people, while stroke sufferers reached 713,783 people in 2018 (Ministry of Health RI, 2018). Based on estimates from the AHA, 42.8% or 100,100,000 million American adults over the age of 20 have a total cholesterol level of 200 mg/dL (5.17 mmol/L) or higher(Dipiro J et al., 2015). According to Jeppsen et al, the higher the triglyceride levels in an individual's blood the higher the risk of developing cardiovascular disease in that individual(Tawfik, 2020).

From various research results, there are approximately 10,000 types of plants that have been utilized by the community for treatment, disease prevention as well as to increase endurance and restore the freshness of the body (Mursito, 2003). Drug use Natural ingredients also tend to be safer than chemical drugs (Hariana, 2007). One of these natural plants is turmeric which contains the main compound curcumin (Ariani, 2017); (Winarto, 2004). Apart from being an antioxidant, curcumin can reduce cholesterol levels due to inhibiting the reabsorption of cholesterol from outside (exogenous) and increasing the enzyme HmgCoA reductase inhibitor so that fat synthesis can run well (Komang and Laksmi, 2014); (Yunarto et al., 2019). The function of curcumin has been proven in a study of dyslipidemic patients in the Sawotratap village area of Sidoarjo Regency who were given turmeric extract for 12 days. Measurement of cholesterol levels was carried out before and after administration of turmeric rhizome extract. Based on the results obtained by using the Paired t-test analysis test, it is stated that there are significant differences in changes in blood lipid levels in research respondents (Gustomi Rima, 2015). The purpose of this study was to determine the effectiveness of the ethanolic extract of turmeric (Curcuma Longa) as an anti-dyslipidemia in male wistar rats given Propylthiouracil (PTU).

II. Review of Literature

Turmeric is the species Curcuma domestica Val (Winarto, 2004), is a traditional medicinal plant (jamu) in Indonesia. The main chemical compounds contained in turmeric are curcuminoids or dyes, which are 2.5 – 6%. Chemical components contained in turmeric rhizome include essential oils, starch, bitter substances, resins, cellulose and some minerals. Turmeric essential oil content is about 3-5% (Winarto, 2004). Turmeric has pharmacological effects such as blood circulation and vital energy, eliminating blockage of menstrual laxatives, anti-inflammatory (anti-inflammatory), facilitating childbirth, antibacterial, facilitating bile secretion (cholagogum), laxative fart (carminative) and moisturizing (astringent) (El-Sayed et al., 2011): (Manarin et al., 2019);(Rezzani, Franco and Rodella, 2019);(Sabale, Modi and Sabale, 2013). Dyslipidemia is defined as a lipid metabolism disorder characterized by an increase or decrease in the lipid fraction in plasma. There are several ways to screen or evaluate anti-dysipidemic activity, namely in vivo methods and in vitro methods (Jijith and Jayakumari, 2018; Untari and Pramukantoro, 2020). In Vivo methods include: Triton-induced dyslipidemic mouse model, PTU, and High-Fat Diet. In Vitro method with Caco-2 strain cells or measurement of HMG-CoA Reductase enzyme inhibitory activity.

III. Research Methods

This study is an experimental study with a Pre-test and Post-test group only control design approach using male wistar rats as experimental animals, March 2021. The sample size in this study was calculated by the Federer formula:

$$(r-1)\ (t-1)\ 15$$

Description:
r: Number of samples in each treatment group
t: Number of treatment groups

$$5(r-1)\ 15$$
$$r-1\ 15/5$$
$$r\ 3\ +1$$
$$r\ 4$$

Based on the results of these calculations, it can be concluded that at least 4 male wistar rats (Rattus norvegicus) are needed in each treatment group. Rat body weight in the range of 180-200gram and have an age between 2-4 months.

Table 1. Aspects of Measurement of Research Variables

No	Variable	How to Measure	Measuring instrument	Measurement Results	Measuring Scale
1.	Dosage of turmeric ethanol extract (Curcuma Longa)	The weight and volume of the extract and the extract vehicle were measured using an analytical balance and a volumetric flask.	Analytical balances and volumetric flasks.	1. Control 2. Standard	ordinal
2.	Lipid Profile	Lipoprotein analysis that can measure blood levels of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides.	Spectroscopic	In mg/dl	Ratio
3.	Total Cholesterol Level	The combined amount of LDL cholesterol, HDL cholesterol, and triglycerides in every deciliter of blood	Autocheck ®	In mg/dl	Ratio
4.	Weight	Weighed using a scale	analytical balance	In grams	Ratio

3.1 Tool

Surgical instruments, laboratory glassware, aluminum foil, blender (Miyako), porcelain cup, desiccator, incubator, slide, cover glass, porcelain crucible, drying cabinet,

microtube, light microscope, analytical balance (Vibra AJ), oral sonde, oven electric (Stork), water bath (Yenaco), tube clamp, test tube rack, rotary evaporator, centrifugator, set of moisture determination apparatus, UV spectrophotometer (Microlet 3000), injection syringe, furnace (Nabertherm), test tube, animal scale (Presica).

3.2 Ingredient

The materials used in this study were turmeric (Curcuma Longa), ethanol, Aquades, Na-CMC (Sodium-Carboxyl methylcellulose), simvastatin, husks, rat food pellets, phytochemical screening reagents, and ketamine.

3.3 Research Procedure

a. Making Turmeric Simplicia (Curcuma Longa)

The identified turmeric (Curcuma Longa) was washed with running water, then drained and spread on parchment paper until the water was absorbed, after which the turmeric (Curcuma Longa) sample was weighed. Then the material is air-dried. The weight of the dry material was weighed. Dry ingredients from turmeric (Curcuma Longa) are ground into powder and form simplicia(Kosasih et al., 2019).

b. Making Turmeric (Curcuma Longa) Ethanol Extract

Turmeric simplicia (Curcuma Longa) was then weighed as much as 200 grams each, then weighedextraction using maceration technique with 96% ethanol solvent. Let stand for 5 days, the container must be protected from direct light or light while stirring frequently, shred, squeeze, wash the dregs with enough liquid to obtain 4 L. Then the simplicia is transferred to a closed vessel, leave in a cool place, protected from light for 2 day. Then this simplicia is filtered. The results obtained were concentrated by using a Rotary Evaporator until most of the solvent evaporated which was then continued by the evaporation process on a water bath until a thick extract was obtained (ethanol extract).Turmeric / Curcuma Longa) (Depkes RI, 1979).

c. Phytochemical Screening

In the phytochemical test study using a modified Fansworth method consisting of identification of phenols, steroids/triterpenoids, terpenoids, saponins, flavonoids, tannins and alkaloids. (Widowati et al., 2016, 2017, 2018).

1. Phenol Identification
   Testing is carried out on the plate in drops, the sample is added with FeCl3 (1% in water/ethanol), if there is a green/red/purple/blue/black color change, it indicates the presence of phenol content.
2. Identification of Steroids/Triterpenoids
   The sample was stored on a drip plate, then added with anhydrous acetic acid until submerged, left for 10-15 minutes, then added 1 drop of concentrated sulfuric acid (H2SO4). If there is a green/blue color change indicates the presence of steroids, the presence of a red/orange precipitate indicates the presence of triterpenoids.
3. Identification of Saponins
   The sample was dissolved in aquadest and shaken vigorously, then observed what happened, the saponin content was indicated by the formation of a stable foam above the solution.
4. Identification of Tannins
   The sample is immersed in taThe reaction tube with 2N HCl solution was then heated on a water bath for 30 minutes and a positive reaction was indicated by the

formation of orange/red in the amyl alcohol layer (top layer).

5. Terpenoid Identification
   The sample is placed on the plate the next drop is added vanillin and H2SO4 solution, a positive reaction is indicated by a color change that occurs to a purple color.
6. Identification of Flavonoids
   The sample is put in the tubereaction containing Mg/Zn granules and then added 2N HCl solution, then incubated for 5-10 minutes and added amyl alcohol solution to the filtrate. A positive reaction is indicated by the formation of a red-orange color.
7. Identification of Alkaloids
   The sample was added with 10% ammonia solution, then extracted with chloroform and formed 2 layers, the bottom layer was transferred to a new test tube and 2N HCl was added then the acid layer (top layer) was transferred back to a new test tube and added Dragendrof solution. A positive reaction is indicated by the formation of a yellow to brick red precipitate.

d. Anti-Dyslipidemic Effect Test

a. Preparation of 0.5% Na CMC Suspension
   As much as 0.5 grams of Na CMC was sprinkled into a mortar containing 10 mL of hot distilled water. Let stand for 15 minutes until a transparent mass is obtained, crushed to form a gel and diluted with a little distilled water, then poured into a 100 mL volumetric flask, plus distilled water to the mark. This suspension will be used further in the next stage as a dispersing medium in making oral suspensions (colloids).(Mutia and Chiuman, 2019)
b. PTU suspension manufacture
   A total of 100 mg of PTU was ground in a mortar to a powder, then 0.5% Na CMC suspension was added and then put into a 10 ml volumetric flask. The volume is made up with 0.5% Na CMC suspension to the limit line(Untari and Pramukatoro, 2020).
c. Turmeric Extract Suspension (Curcnuma Longa).
   A total of 1.2 grams of turmeric extract (Curcnuma Longa) was put into a mortar and added 0.5% Na CMC suspension little by little while grinding until homogeneous and then put into a 10 mL volumetric flask. The volume was made up with 0.5% Na CMC suspension to the mark line.(Mutia and Chiuman, 2019).
d. Simvastatin Suspension Manufacturing
   A total of 10 mg of simvastatin was ground in a mortar to a powder, then 0.5% Na CMC suspension was added and then put into a 25 mL volumetric flask. The volume was made up with 0.5% Na CMC suspension to the mark line(Fouad and Jresat, 2013; Aldahmash and El-Nagar, 2016).
e. Induction of Dyslipidemia in Experimental Animals
   The induction process was carried out by giving Propylthiouracil (PTU) to experimental animals for 14 days. Propylthiouracil (PTU) is given as an oral suspension at a dose of 12.5 mg/day (1.25 ml/day) in 2 divided doses.(Subhawa Harsa, 2014; Untari and Pramukantoro, 2020)
f. Testing on Test Animals
   A week before the intervention was carried out on all experimental animals, the experimental animals were first acclimatized to a laboratory environment. After that, all wistar rats were induced using Propylthiouracil (PTU), except from the

normal group. After 14 days, the test animals with total cholesterol 240 mg/dl were declared to have dyslipidemia. However, before measuring total cholesterol levels, all rats were fasted for at least 8 hours. The test animals were divided into 6 groups and each consisted of 4 experimental animals. Doses of turmeric ethanol extract and simvastatin as a standard group, were determined based on previous studies(Olayinka et al., 2014; Batubara, Sabri and Tanjung, 2017; Worotikan, Tuju and Kawuwung, 2017; Abarikwu et al., 2020). The treatment experienced by each rat in the group was as follows:

Table 2. Description of the Treatment of Each Group

No	Test Group	Treatment
1.	Normal	Test animals were not given any particular treatment and were only given food and drink on an ad libitium basis.
2.	Control	Test animals were given 1 ml of 0.5% Na CMC suspension once a day for 14 days. Food and drinks are provided ad libitum.
3.	Standard (25 mg/kgBW)	Test animals were given simvastatin oral suspension 5 ml/kg once a day for 14 days. Food and drinks are provided ad libitum.
4.	Turmeric Extract (Curcuma Longa) - I (300 mg/ kgBW)	Test animals were given Turmeric Extract (Curcuma Longa) at a dose of 2.5 ml/kgBW once a day for 14 days. Food and drinks are provided ad libitum.
5.	Turmeric Extract (Curcuma Longa) - II (600 mg/kgBW)	Test animals were given Turmeric Extract (Curcuma Longa) at a dose of 5 ml/kgBW once a day for 14 days. Food and drinks are provided ad libitum.
6.	Turmeric Extract (Curcuma Longa) - III (1200 mg/kgBW)	Test animals were given Turmeric Extract (Curcuma Longa) at a dose of 10 ml/kgBW once a day for 14 days. Food and drinks are provided ad libitum.

e. Measurement of Lipid Profile Parameters

Before taking blood, rats were fasted for at least 8 hours before taking blood. Blood was drawn by direct withdrawal from the rat heart as much as 1 ml. It was put into a microtube and allowed to stand for ± 20 minutes. Then the blood was centrifuged at 3000 rpm for 15 minutes to obtain rat blood serum. Lipid profiling was determined by the colorimetric method. Lipid profile examination was carried out at the Health Laboratory, North Sumatra Provincial Health Office.

g. Measurement of SGOT and SGPT Biochemical Parameters

Blood was drawn by direct withdrawal from the rat heart as much as 1 ml. It was put into a microtube and allowed to stand for ± 20 minutes. Then the blood was centrifuged at 3000 rpm for 15 minutes to obtain rat blood serum. The determination of SGOT and SGPT levels is based on enzymatic reactions using the Dyasis® reagent kit. The procedure for determining the activity of SGOT and SGPT catalysts is based on the working procedure of Dyasis®. SGOT and SGPT examinations were carried out at the Health Laboratory, North Sumatra Provincial Health Office.

3.4 Data Analysis

The research data were then analyzed using the SPSS 25 program. The research data were analyzed descriptively (Central tendency and Dyspersion) from the research data in the form of lipid profiles (LDL, HDL, Total Cholesterol, and Triglycerides), color, texture,

weight. Then the research data in the form of lipid profiles were analyzed by One-Way Anova if the data were normally distributed with a follow-up test in the form of the Post Hoc Tukey HSD test to see significant differences between treatments. However, as an alternative test if the data is not normally distributed, the Kruskall-Wallis test is used as an alternative test.

IV. Discussion

4.1 Results

a. Extract Characteristics

After Extraction was carried out by maceration method on samples of ethanolic turmeric (Curcuma Longa) and the characteristics of the extract were as follows.

Table 3. Turmeric (Curcuma Longa) Ethanol Extract Characteristics

Characteristics	Mark
Fresh Simplicia Weight (gr)	500 gr
Dry Simplicia Powder Weight (gr)	214 gr
Solvent Volume (ml)	2120 ml
Extract Weight (gr)	15.22 gr
Yield (%)	7.22%

From data from the table above, it can be seen that from 500 grams of turmeric (Curcuma Longa), 15.22 grams of extract were found. Thus, the yield obtained from the ethanol extract of turmeric (Curcuma Longa) was 7.22%.

b. Phytochemical Screening

Results Phytochemical screening on samples of turmeric ethanol extract (Curcuma Longa) can be seen in the following table.

Table 4. Results of Phytochemical Screening of Turmeric Ethanol Extract (Curcuma Longa)

Phytochemicals	Reactor	Results
Alkaloids	Bouchardart	+
	Mayer	+
	Dragondrop	-
	Wagner	+
Saponins	Aquadest + Alcohol 96%	-
Flavonoids	FeCl3 5%	+
	Mg(s) + HCl(p)	-
	NaOH 10%	-
	H2SO4 (p)	-
Tannins	FeCl3 1%	+
Steroids and Terpenoids	Salkowsky	-
	Liberman Bouchard	+

From data from the table above, it can be seen that the ethanol extract of turmeric (Curcuma Longa) contains several phytochemical compounds including Alkaloids, Saponins, Flavonoids, Tannins, and Steroids and Terpenoids.

c. Evaluation of Anti-Dyslipidemic Effect

All parameters evaluated in this study including body weight, total cholesterol, lipid profile, levels of SGOT, and SGPT were analyzed for normality of the data using the

Shapiro-Wilk test. The results of the normality analysis can be seen in the table below.

Table 5. Results of Data Normality Test with Shapiro-Wilk Test on All Research Parameters

Parameter		P value	Data Distribution
Weight		0.399	Normal
Total Cholesterol Before Induction		< 0.05	Abnormal
Total Cholesterol After Induction		< 0.05	Abnormal
Lipid Profile After Treatment	Total Cholesterol	0.445	Normal
	Triglycerides	0.004	Abnormal
	HDL levels	< 0.05	Abnormal
	LDL levels	0.143	Normal
SGOT level		< 0.05	Abnormal
SGPT level		0.056	Normal

From the table data above, it can be seen that the data on body weight, total cholesterol and LDL levels from the lipid profile after treatment, and SGPT levels had normal data distributions, while other parameters included: total cholesterol before and after induction, triglyceride levels, HDL levels, and SGOT levels were not normally distributed. Based on the data distribution, data with normal data distribution were analyzed using parametric statistics, while non-normal data were analyzed using non-parametric statistics.

d. Weight

To uniform the weight of the mice used in this study, all the mice used in this study were weighed first. Then a comparison was made on the whole body weight of the rats. The results of this comparison can be seen in the following table.

Table 6. Comparison of Initial Body Weight of Rats in All Treatment Groups

Treatment Group	Weight (grams)		P value
	mean	SD	
Normal	235.00	37.75	0.968
Standard	240.70	15.62	
Control	249.00	23.77	
Turmeric (Curcuma Longa) Ethanol Extract I	247.00	25.50	
Turmeric (Curcuma Longa) Ethanol Extract -II	234.50	24.52	
Turmeric (Curcuma Longa) Ethanol Extract -III	240.55	13.87	

From data the table above can be seen that the P value > 0.05 (P value = 0.968) which means that there is no significant difference in the initial body weight of the mice used in this study. The weight range of rats used in this study ranged from 210-300grams which were evenly distributed in each treatment group.

e. Total Cholesterol

In evaluating the anti-dyslipidemic effect of turmeric ethanol (Curcuma Longa), a high-fat diet was administered to the control group, standard, turmeric ethanol extract (Curcuma Longa)-I, II, and III. Before and after administration of PTU, total cholesterol in all mice was measured and all data on total cholesterol were analyzed by non-parametric statistics. The results of the analysis can be seen in the following table.

Table 7. Comparison of Total Cholesterol Before and After Administration of PTU (Propylthiouracil) in All Treatment Groups

Treatment Group	Total Cholesterol (mg/dL)	
	Before Induction	**After Induction**
Normal	117.00 (110-115)	118.50 (111-123)b
Standard	11,300 (110-117)	211.00 (209-211)a
Control	116.50 (110-115)	210.00 (210-214)b
Turmeric (Curcuma Longa) Ethanol Extract -I	116.00 (110-115)	210.50 (208-212)b
Turmeric (Curcuma Longa)-II . Ethanol Extract	112.50 (100-110)	210.00 (209-214)b
Turmeric (Curcuma Longa) Ethanol Extract-III	117.00 (117-125)	209.50 (208-214)b
P value	**0.882**	**0.027**

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

From data the table above can be seen that before being given a high-fat diet, the total cholesterol of rats before being given a high-fat diet in all treatment groups did not show a significant difference (P value = 0.882). This shows that the total cholesterol data of rats before being given a high-fat diet is uniform. However, the total cholesterol in all groups of rats after being given a high-fat diet showed a different distribution, where only the control group, standard, Turmeric extract (Curcuma Longa)-I, II, and III showed uniform total cholesterol.

f. Lipid Profile

On At the end of the study, all mice were terminated for blood collection and analysis of lipid profile and liver function (SGOT/SGPT). Comparison of lipid profiles in all rat treatment groups can be seen in the table below.

Table 8. Comparison of Lipid Profiles in All Treatment Groups of Rats

Treatment Group	Lipid Profile			
	Total Cholesterol*	**Triglycerides****	**LDL***	**HDL****
Normal	133.00 ± 2.40a	97.50 (97-100)a	53.50 ± 1.64a	61.50 (61-64)a
Standard	147.50 ± 0.58b	103.00 (101-105)b	63.00 ±1.27b	60.50 (60-63)a
Control	178.50 ± 6.05c	167.00 (162-179)c	107.20 ±3.60c	28.50 (37-45)b
Turmeric Ethanol Extract I	168.25 ± 1.50d	133.50 (133-135)d	83.75 ±2.62d	57.50 (56-59)b
Turmeric Ethanol Extract II	163.25 ± 2.22e	120.50 (119-122)e	77.50 ± 1.29e	61.50 (61-63)a
Turmeric Ethanol Extract III	151.70 ± 0.95e	110.00 (109-112)f	68.50 ±1.28f	61.00 (60-62)a
P value	**< 0.05**	**0.027**	**< 0.05**	**0.027**

*Data is displayed as Mean ± SD. The P value was obtained from 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

From data the table above can be seen that all lipid profile data in all treatment groups showed significant differences.

a. Total cholesterol in all rat treatment groups showed a significant difference, this can be seen from the P value < 0.05. The lowest average total cholesterol was found in the normal group, namely 133.00 ± 2.40 mg/dL, followed by the standard group at 147.50 ± 0.58 mg/dL, the Turmeric (Curcuma Longa) ethanol extract group I, II, III, and the group with total cholesterol. the highest was the control group at 178.50 ± 6.02 mg/dL;
b. Triglyceride levels in all treatment groups also showed significant differences, this can be seen from the P value < 0.05 (P value = 0.027). The tendency for the lowest triglyceride levels was found in the normal group, namely 97.50 mg/dL, followed by

the standard group at 103.00 mg/dL, the Turmeric (Curcuma Longa) ethanol extract group I, II, III, and the group with the highest triglyceride levels was the control group of 167.00 mg/dL.

c. LDL levels also showed significant differences in all treatment groups, this can be seen from the P value < 0.05. The lowest average LDL level was found in the normal group, namely 53.50 ± 1.64 mg/dL, followed by the standard group at 63.00 ± 1.27 mg/dL, the Turmeric (Curcuma Longa) ethanol extract group I, II, III, and the group with LDL levels. the highest was the control group at 107.50 ± 3.60 mg/dL.
d. HDL levels also showed significant differences in all treatment groups, this can be seen from the P value < 0.05 (P value = 0.027). The tendency for the highest HDL levels was found in the normal group, namely 61.50 mg/dL, followed by the standard group at 60.50 mg/dL, the Turmeric extract group (Curcuma Longa) I, II, III, and the group with the lowest HDL levels was the control group at 28.50. mg/dL.

g. Liver Function

Other parameters are also assessed in all groups of rats at the end of the study was liver function, namely: SGOT and SGPT levels. Comparison of SGOT and SGPT levels in all rat treatment groups can be seen in the table below.

Table 9. Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Group	**SGOT Level (U/L)**	**SGPT level (U/L)**
Normal	27.50 (26-30)a	47.50 ± 1.50a
Standard	110.00 (106-110)b	171.00 ± 1.28b
Control	167.50 (162-170)c	97.25 ± 1.50c
Turmeric (Curcuma Longa) Ethanol Extract -I	117.50 (116-120)d	100.75±3.56d
Turmeric (Curcuma Longa)-II . Ethanol Extract	121.00 (120-124)e	115.00 ± 4.50e
Turmeric (Curcuma Longa) Ethanol Extract-III	129.50 (128-130)f	142.00 ± 2.08b
P value	**0.027**	**< 0.05**

*Data is displayed as Mean ± SD. The P value was obtained from 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

From data the table above shows that the levels of SGOT and SGPT in all rat treatment groups showed significant differences, this can be seen from the P value < 0.05. The tendency for the highest SGOT levels was found in the control group, namely 167.50 U/L and the lowest in the normal group, namely 27.50 U/L. Meanwhile, a similar picture was found in SGPT levels, the group with the highest SGPT levels was found in the standard group, namely 170.50 U/L and the lowest was found in the normal group, namely 47.50 U/L.

4.2 Discussion

The results of this study showed that the ethanol extract of turmeric (Curcuma Longa) showed a significant improvement in lipid profile at the end of the study. Turmeric ethanol (Curcuma Longa) at the highest dose showed the most optimal improvement in lipid profile. This can be seen from the decrease in total cholesterol, triglyceride, and LDL levels as well as the increase in HDL levels from the Turmeric (Curcuma Longa)-II and III ethanol group. However, this improvement in lipid profile in the Turmeric (Curcuma Longa)-III ethanol group of mice did not exceed the improvement shown in the standard group. The anti-dyslipidemic effect of Turmeric (Curcuma Longa) ethanol extract may be related to the content of various phytochemicals in turmeric rhizome.

Several studies have demonstrated the potential of these phytochemicals as anti-dyslipidemia. The content of polyphenols can cause down-regulation of modulation of pro-inflammatory cell signals such as nuclear factor-κB, activated protein-1, and mitogen-activated protein kinase through inhibition of the arachidonic acid cascade and eicosanoids derivatives. Another possible mechanism for the anti-dyslipidemic effect of polyphenolic compounds is the regulation of gut microbiota. These polyphenolic compounds in the intestine will interact with the gut microbiota thereby increasing various beneficial metabolite products such as short chain free fatty acids, as well as intestinal microbiota such as Akkermansia municiphilia sp. restore inflammatory conditions in the intestine, improve intestinal permeability, and insulin sensitivity. Furthermore,(Sun, Wang and Qin, 2018; Feldman et al., 2021).

Other studies that discuss the anti-dyslipidemic effect of turmeric ethanol are still limited, but the results of Ardhani's research (2017), entitled The Effectiveness of Turmeric Extract (Curcuma domestica) as Non-Pharmacological Therapy for Dyslipidemia and Antiatherosclerosis, states that giving turmeric extract can be a therapy non-pharmacological dyslipidemia and as an antiatherosclerosis agent. Turmeric extract contains the compound curcumin which is an antioxidant. Curcumin can reduce LDL oxidation which plays a role in foam cell formation, suppresses inflammatory processes in blood vessels, and protects blood vessel endothelium from free radicals (Ardhani et al., 2017). Apart from being an antioxidant, curcumin can reduce cholesterol levels due to inhibiting the reabsorption of cholesterol from outside (exogenous) and increasing the enzyme Hmg-CoA reductase inhibitor so that fat synthesis can run well.(Komang and Laksmi, 2014). Treatment and prevention of disease with curcumin is one of the therapeutic modalities that is not inferior to the pharmacological approach (Shishodia et al., 2005).

In addition, turmeric ethanol extract, also significantly reduced levels of SGOT and SGPT compared to the control group. This decrease in SGOT and SGPT levels is associated with improvement in Non-Alcoholic Fatty Liver Disease (NAFLD). Several studies have shown that NAFLD is a risk factor for the development of atherosclerosis. This is because NAFLD causes dysfunction of the vascular endothelium. Thong and Quynh (2021) reported that both SGOT and SGPT correlated with the occurrence of NAFLD, but the use of SGOT and SGPT separately could show errors in confirming mild NAFLD. In severe cases of NAFLD, SGOT will increase slightly and in mild cases SGOT levels can be found in normal amounts. Therefore,(Thong and Quynh, 2021). In this study, the levels of SGOT and SGPT in the group of rats receiving ethanol extract of turmeric (Curcuma Longa) were lower than the levels of SGOT and SGPT in the control group. This shows that turmeric ethanol extract (Curcuma Longa)- can protect liver tissue from NAFLD compared to the group that did not receive turmeric ethanol (Curcuma Longa)-. However, the possibility of mild NAFLD in the group of rats receiving turmeric ethanol (Curcuma Longa) could not be ruled out.

V. Conclusion

As for the conclusion that can be drawn from the results of this study is that the ethanol extract of turmeric (Curcuma Longa) III (151.70 ± 0.95 mg/dl) can significantly reduce total cholesterol compared to the control group (178.50 ± 6.05 mg/dl). (P value < 0.05). The ethanol extract of turmeric (Curcuma Longa) III (110.00± (109-112) mg/dl) was able to significantly reduce triglyceride levels compared to the control group (167.00 (162-179) mg/dl). (P value = 0.027). The ethanol extract of turmeric (Curcuma Longa) III (68.50

± 1.28 mg/dl) could significantly reduce LDL levels compared to the control group (107.20 ± 3.60 mg/dl). (P value < 0.05). The ethanol extract of turmeric (Curcuma Longa) III, (61.00 (60-62) mg/dl) could significantly increase HDL levels compared to the control group (28.50 (37-45) mg/dl). (P value = 0.027).

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