BloEx - Journal
Britain International of
EXACT Sciences Journal
Publish: | January - May - September |
E-ISSN: 2686-1208
P-ISSN: 2686-1216
http://biarjournal.com/index.php/bioex

Anti-Dislipidemia Effectiveness Test of Turmeric Ethanol Extract (Curcuma Longa) in Male Wistar Mice Given a High-Fat Diet

Wang Lei[1], Florenly[2], Liena[3], Fioni[4]
[1,2,3,4]Master of Clinical Medicine, Faculty of Medicine, Universitas Prima Indonesia
Email: ly@unprimdn.ac.id

Abstract:

Dyslipidemia is a condition of increasing levels of Low Density Lipoprotein (LDL), cholesterol in the blood, or triglycerides in the blood that can be accompanied by a decrease in levels of High Density Lipoprotein (HDL). Herbal products have been used since long ago in the medical world, one of which is curcuma longa root. The main compound of turmeric is curcumin which can lower cholesterol levels due to inhibiting cholesterol reabsorbtion from the outside and increase the enzyme HmgCoA reductase inhibitor so that fat synthesis can run properly. The purpose of this study was to find out the effectiveness of turmeric ethanol extract (Curcuma Longa) as an anti-dyslipidemia in male wistar rats given a high-fat diet. This experimental study with the pre-test and post-test group only control design approach was conducted in January 2021, at the Herbarium Medanese FMIPA USU. The size of the sample was calculated by Federer's formula, with at least 4 mice in each treatment group. The results and conclusions of turmeric ethanol (Curcuma Longa) III (150.20 ± 0.90 mg/dl) significantly decreased total cholesterol compared to the control group (177.50 ± 6.02mg/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 (166.50 (160-175) mg/dl), (value P = 0.024). Turmeric ethanol extract (Curcuma Longa) III (66.50 ± 1.25 mg/dl) significantly lowered LDL levels compared to the control group (106.20 ± 3.50 mg/dl), (P value < 0.05). Turmeric ethanol extract (Curcuma Longa) III, (60.00 (59-61) mg/dl) can significantly increase HDL levels compared to the control group (27.00 (33-39) mg/dl), (Value P = 0.024). Turmeric ethanol extract (Curcuma Longa) III significantly lowered SGOT (Value = 0.024) and SGPT (Value P < 0.05) compared to the control group.

Keywords:
dyslipidemia; turmeric; high-fat diet

I. Introduction

Dyslipidemia is a condition of increasing levels of Low Density Lipoprotein (LDL), cholesterol in the blood, or triglycerides in the blood that can be accompanied by a decrease in levels of High Density Lipoprotein (HDL) (Hardiansyah, 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), and become one of the risk factors for atherosclerosis and coronary heart disease (CHD). (D'Agostino et al., 2008). The number of heart disease sufferers in Indonesia reached 1.017 million people (Kemenkes RI, 2018), and globally the cause of death of 17.8 million in 2017 (Wulansari, 2020). 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); (Dipiro J et al.,

2015). Dyslipidemia can be caused by daily dietary intake that can increase cholesterol levels, especially LDL, such as fat.

Herbal products have been used since long ago in the medical world, one of which is curcuma longa root. The main compound of turmeric is curcumin (Nabofa et al., 2018). Some of the benefits of turmeric from the results of research are turmeric is antioxidant (Wanninger et al., 2015); (Razavi, 2021); (Razavi, 2021), anti-inflammatory (Manarin et al., 2019); (Setiadi, Khumaida and Wahyuning Ardie, 2017); (Kocaadam and Şanlier, 2017), Anti-cancer (Hartati, 2013); (Razavi, 2021). Curcumin can also lower cholesterol levels due to inhibiting the reabsorbtion of cholesterol coming from outside (exogenous) and increase the enzyme HmgCoA reductase inhibitor so that fat synthesis can run properly (Komang and Laksmi, 2014); (Yunarto et al., 2019). Research (Gustomi Rima, 2015), In the village area of Sawotratap Sidoarjo Regency in people with dyslipidemia, stated that there was a significant difference from changes in blood fat levels in study respondents given turmeric extract for 12 days. The purpose of this study was to find out the effectiveness of turmeric ethanol extract (Curcuma Longa) as an anti-dyslipidemia in male wistar rats given a high-fat diet.

II. Review of Literature

Turmeric has pharmacological effects such as, blood and vital energy, removing menstrual straighteners, anti-inflammatory (anti-inflammatory), facilitating labor, antibacterial, smoothing bile production (kolagogum), fart straighteners (carminative) and moisturizer (astringent) (El-Sayed et al., 2011). The main compounds contained in turmeric are curcumin and essential oils. These compounds have the role of antioxidants, antitumor and anticancer, antipykun, lowering levels of fat and cholesterol in the blood and liver, antimicrobial, antiseptic and anti-inflammatory (Manarin et al., 2019): (Rezzani, Franco and Rodella, 2019): (Sabale, Modi and Sabale, 2013). There are several ways to screen or evaluate anti-dysipidemia activities, namely in vivo methods and in vitro methods. In vivo methods that can be used in evaluating anti-dyslipidemia, include: triton-induced dislipidemic mouse models, PTU, and a High-Fat Diet (Jijith and Jayakumari, 2018; Untari and Pramukantoro, 2020). A high-fat diet can lead to increased fat cell size (hypertrophy) and an increase in cell count (hyperplasia) (Ge et al., 2018); (Mawarti, Ratnawati and Lyrawati, 2012).

III. Research Methods

The study was experimental with the Pre-test and Post-test group only control design approach conducted January 2021, at the Herbarium Medanese FMIPA USU, the Pharmacognosive Laboratory of the FACULTY of Pharmacy USU, and the LABORATORY of Pharmaceutical Pharmacology USU. The test animal is a male wistar rat weighing in the range of 180-200grams and has a rat age between 2-4 months. The size of the sample is calculated with Federer's formula, concluding that at least 4 rats are needed in each treatment group.

3.1 Tool

Surgical tools, laboratory glass tools, aluminum foil, blender (Miyako), porcelain cups, deikators, incubators, glass objects, cover glass, porcelain crusts, dryer cabinets, microtubes, light microscopes, analytical balance sheets (Vibra AJ), oral sonde, electric oven (Stork), water handler (Yenaco), tube clamps, test tube racks, rotary evaporators, centriofigators, a set of water content determination tools, UV spectrophotometers (Microlet 3000), injection spuits, tanurs (Nabertherm), test tube, animal scales (Presica).

3.2 Material

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

3.3 Research Procedure

Samples of turmeric (Curcuma Longa) used in this study were obtained from one of the traditional markets in Medan City. Then the turmeric sample (Curcuma Longa) was later identified at the Herbarium Medanense FMIPA USU. Turmeric (Curcuma Longa) which has been identified washed thoroughly with running water, then lined and then spread on paper until the water is absorbed, after which the turmeric sample (Curcuma Longa) is weighed. Then the material is dried by winding. The weight of the dry material is weighed. The dry ingredients of turmeric (Curcuma Longa) are mashed to powder and form simplisia (Kosasih *et al.*, 2019).

Simplisia turmeric (Curcuma Longa) is then weighed as much as 200 grams each, then extracted using a maceration technique with a 96% ethanol solvent. Silenced for 5 days, the container should be protected from direct light or light while often stirred, stirring, squeeze, wash the dregs with sufficient cleaning fluid until obtained 4 L. Then simplisia is transferred into a closed vessel, leave it in a cool place, protected from light for 2 days. Then this simplisia is filtered. The results obtained are compressed using a Rotary Evaporator tool until most of the solvent evaporates which then continues the evaporation process on top of the water handler until a viscous extract (turmeric ethanol extract/ Curcuma Longa) (Depkes RI, 1979).

In the phytochemical test study used modifications to fansworth's way consisting of identification of phenols, steroids/ triterpenoids, terpenoids, saponins, flavonoids, tannins and alkaloids (Widowati *et al.*, 2016, 2017, 2018).

3.4 Testing for Anti-Dyslipidemia

a. Na CMC Suspension Manufacturing 0.5%

A total of 0.5grams of Na CMC is sprinkled into a lumpang containing 10 mL of hot distilled water. Let stand for 15 minutes until a transparent period is obtained, eroded until a gel is formed and diluted with a little distilled water, then poured into the pumpkin of course 100 mL, plus distilled water to the limit of the mark. This suspension will be used further at a later stage as a dispersal medium in making oral suspense (Colloidal) (Mutia and Chiuman, 2019).

b. Manufacture of Hyperchoestrolemia Feed Suspension

The suspension is made by mixing 300 grams of animal fat into 100 ml of aquadest and 200 grams of poultry egg yolks into 1 ml of Na-CMC 0.5% (Harsa, 2014).

c. Turmeric Extract Suspension (Curcnuma Longa)

A total of 1.2 grams of turmeric extract (Curcuma Longa) is put into the lumpang and added a 0.5% Na CMC suspension little by little while being gnawed until homogeneous and then put into the pumpkin of course 10 mL. The volume is sufficient with a 0.5% Na CMC suspension up to the mark line (Mutia and Chiuman, 2019).

d. Simvastatin Suspension Manufacturing

As much as 10 mg of simvastatin is gnawed in lumpang until it becomes powder, then added a 0.5% Na CMC suspension and then put into a pumpkin of 25 mL. Volume is

sufficient with a 0.5% Na CMC suspension up to the mark line (Fouad and Jresat, 2013; Aldahmash and El-Nagar, 2016).

e. Induction of Dyslipidemia in Animals

The induction process is done by giving a high-fat diet to animals try for 14 days. A high-fat diet is given with a high-fat feed suspension with a dose of 15 gr/ kgBB for animal fat suspension and 10 gr / kgBB for poultry egg yolk suspension (Harsa, 2014; Untari and Pramukantoro, 2020).

f. Testing on Test Animals

A week before the intervention on all animals, the animals try to first be carefully characterized by the laboratory environment. After that, the entire wistar mouse was induced using hyperchoestrol feed, except from the normal group. After 14 days, test animals with total cholesterol ≥ 240 mg/dl were declared to have dyslipidemia. However, before measuring total cholesterol levels, all mice were satisfied for at least 8 hours. The test animals are divided into 6 groups and each consists of 4 experimental animals. Dosage of turmeric ethanol extract and simvastatin as standard group, 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 of the mice in the group is as follows:

Table 1. Overview of the Treatment of Each Group

No	Test Group	Treatment
1.	Normal	Test animals are not given certain treatment and are only fed and drank on an ad libitium basis.
2.	Control	Test animals were given a 1 ml Na CMC suspension of 0.5% once a day for 14 days. Food and drink are given ad libitum.
3.	Standard (25 mg/kgBB)	Test animals were given a 5 ml/kgBB oral simvastatin suspension once a day for 14 days. Food and drink are given ad libitum.
4.	Turmeric Extract (Curcuma Longa) - I (300 mg/ kgBB)	Test animals were given 2.5 ml/kgBB of turmeric ethanol extract once a day for 14 days. Food and drink are given in ad libitum.
5.	Turmeric Extract (Curcuma Longa) - II (600 mg/kgBB)	Test animals were given turmeric ethanol extract (Curcuma Longa) dose of 5 ml/kgBB once daily for 14 days. Food and drink are given ad libitum.
6.	Turmeric Extract (Curcuma Longa) - III (1200 mg/kgBB)	Test animals were given turmeric ethanol extract (Curcuma Longa) dose of 10 ml/kgBB once a day for 14 days. Food and drink are given ad libitum.

Information: BB (Weight).

Before the blood draw, the mice were satisfied at least 8 hours before the blood draw. Blood collection is done by direct withdrawal from the heart of the mouse as much as 1 ml. Put in a microtube and let stand ± 20 minutes. Then the blood was dyscentive at a speed of 3000 rpm for 15 minutes to get the blood serum of the mice. The determination of lipid profiles is determined by a colorimetric method. Examination of lipid profiles is carried out at

the Health Laboratory, North Sumatra Provincial Health Office. Blood collection is done by direct withdrawal from the heart of the mouse as much as 1 ml. Put in a microtube and let stand ± 20 minutes. Then the blood was dyscentive at a speed of 3000 rpm for 15 minutes to get the blood serum of the mice. The determination of SGOT and SGPT levels is based on enzymatic reactions using Dyasis reagent kits®. Procedures for determining the activity of SGOT and SGPT catalysts based on the working procedures of Dyasis®. SGOT and SGPT examinations were conducted at the Health Laboratory, North Sumatra Provincial Health Office. The data was analyzed descriptively (Central tendency and Dyspersi) from the study results data in the form of lipid profiles (LDL, HDL, Total Cholesterol, and Triglycerides), color, texture, weights. Then the data in the form of lipid profiles is analyzed with One-Way Anova if the data is distributed normally with follow-up tests in the form of Post Hoc Tukey HSD tests to see real differences between treatments. However, as an alternative test if the distributed data is not normal, the Kruskall-wallis test is used as an alternative test.

IV. Discussion

4.1 Results

a. Characteristics of Extract

After extraction by maceration method against samples of turmeric ethanol (Curcuma Longa) found the following characteristics of the extract.

Table 2. Characteristics of Turmeric Ethanol Extract (Curcuma Longa)

Characteristic	Value
Fresh Simplisia Weight (gr)	500 gr
Dry Simplisia Powder Weight (gr)	213 gr
Solvent Volume (ml)	2120 ml
Extract Weight (gr)	15,19 gr
Yield (%)	7.20%

From the table data above it can be seen that from 500 grams of turmeric (Curcuma Longa) found an extract of 15.19 grams. Thus, the amount of yield obtained from turmeric ethanol extract (Curcuma Longa) is 7.20%.

b. Phytochemical Screening

The results of phytochemical screening on samples of turmeric ethanol extract (Curcuma Longa) can be seen in the following table.

Table 3. Phytochemical Screening Results of Turmeric Ethanol Extract (Curcuma Longa)

Phytochemicals	Reagent	Value
Alkaloid	Bouchardart	+
	Mayer	+
	Dragondroff	-
	Wagner	+

Saponin	Aquadest + Alcohol 96%	-
Flavonoid	FeCl3 5%	+
	$Mg_{(s)}$ + $HCl_{(p)}$	-
	NaOH 10%	-
	$H_2SO_{4\ (p)}$	-
Tanin	$FeCl_3$ 1%	+
Steroid dan Terpenoid	Salkowsky	-
	Liberman Bouchard	+

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

c. Evaluation of Anti-Dyslipidemia Effects

All parameters evaluated in the study included body weight, total cholesterol, lipid profile, SGOT levels, and SGPT analyzed the normality of the data using the Shapiro-Wilk test. The results of the normality analysis can be seen in the table below.

Table 4. Data Normality Test Results with Shapiro-Wilk Test of All Research Parameters

Parameter		**Value P**	**Data Distribution**
Weight		0.389	Normal
Total Cholesterol Before Induction		< 0.05	Abnormal
Total Cholesterol After Induction		< 0.05	Abnormal
Lipid Profile After treatment	Total Cholesterol	0.449	Normal
	Trigliserida	0.003	Abnormal
	HDL levels	< 0.05	Abnormal
	LDL levels	0.148	Normal
SGOT rate		< 0.05	Abnormal
SGPT rate		0.058	Normal

From the table data above it can be seen that the data on weight, total cholesterol and LDL levels of the lipid profile after treatment, and SGPT levels have a normal data distribution, while other parameters include: total cholesterol before and after induction, triglyceride levels, HDL levels, and abnormally distributed SGOT levels. Based on the distribution of these data, the data with normal data distribution is analyzed with parametric satistics while abnormal data is analyzed with non-parametric statistics. To uniformize the weight of the mice used in the study, all the mice used in the study weighed their weight first. Then a comparison was made on the entire weight of the mice. The results of the comparison can be seen in the following table.

Table 5. Comparison of Early Weight of Mice in the Entire Treatment Group

Treatment Group	Weight (gram)		P Value
	Mean	SD	
Normal	234.50	37.74	0.962
Standard	240.80	15.62	
Control	245.50	23.77	
Turmeric Ethanol Extract (Curcuma Longa) I	247.50	25.50	
Turmeric Ethanol Extract (Curcuma Longa) II	233.50	24.50	
Turmeric Ethanol Extract (Curcuma Longa) III	240.55	14.87	

From the table data above can be seen the value of P > 0.05 (Value P = 0.962) which means there is no significant difference to the initial weight of the mice used in this study. The weight span of the mice used in the study ranged from 214-300grams evenly spread across each treatment group.

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

Table 6. Comparison of Total Cholesterol before and after High-Fat Diet in All Treatment Groups

Treatment Group	Total Cholesterol (mg/dL)	
	Before induction	**After induction**
Normal	115.00 (110-115)	117.00 (110-123)[b]
Standard	112.50 (110-110)	210.00 (209-212)[a]
Control	115.50 (110-115)	210.00 (210-210)[b]
Turmeric Ethanol Extract (Curcuma Longa) I	116.50 (110-115)	215.50 (206-212)[b]
Turmeric Ethanol Extract (Curcuma Longa) II	113.50 (100-110)	210.00 (204-216)[b]
Turmeric Ethanol Extract (Curcuma Longa) III	116.50 (115-125)	201.50 (203-215)[b]
P Value	**0.867**	**0.024**

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

From the table data above it can be seen that before being given a high-fat diet, the total cholesterol of mice before the administration of a high-fat diet in the entire treatment group showed no significant difference (Value P = 0.867). This showed that the total cholesterol data of mice before being given a high-fat diet was uniform. However, total cholesterol in the entire group of mice after a high-fat diet showed a different distribution,

with only the control group, standard, turmeric extract (Curcuma Longa)-I, II, and III showing uniform total cholesterol.

At the end of the study, all of the mice were terminated for blood and analyzed lipid profile and liver function (SGOT/SGPT). Comparison of plipid profiles across the mouse treatment group can be seen in the table below.

Table 7. Comparison of Lipid Profiles in the Entire Group of Rat Treatments

Treatment Group	Profil Lipid			
	Total Kolestrol*	**Trigliserida****	**LDL***	**HDL****
Normal	132.00 ± 2.30a	96.50 (97-100)a	52.00 ± 1.60a	60.00 (61-63)a
Standard	146.00 ± 0.52b	102.00 (101-105)b	62.00 ±1.20b	59.50 (60-63)a
Control	177.50 ± 6.02c	166.50 (160-175)c	106.20 ±3.50c	27.00 (33-39)b
Turmeric Ethanol Extract (Curcuma Longa) I	178.25 ± 1.50d	133.50 (133-135)d	83.75 ±2.62d	57.50 (56-59)b
Turmeric Ethanol Extract (Curcuma Longa) II	163.25 ± 2.22e	120.50 (119-122)e	77.50 ± 1.29e	61.50 (61-63)a
Turmeric Ethanol Extract (Curcuma Longa) III	150.20 ± 0.90e	110.00 (109-112)f	66.50 ±1.25f	60.00 (59-61)a
P Value	**< 0.05**	**0.024**	**< 0.05**	**0.024**

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

a. Total cholesterol in the entire treatment group of mice showed a significant difference, this can be seen from the value of P < 0.05. The lowest average total cholesterol was found in the normal group of 132.00 ± 2.30 mg/dL, followed by the standard group of 146.00 ± 0.52 mg/dL, the turmeric ethanol extract group (Curcuma Longa) I, II, III, and the group with the highest total cholesterol was the control group of 178.25 ± 1.50 mg/dL.;
b. Triglyceride levels in the entire treatment group also showed significant differences, this can be seen from the value of P < 0.05 (Value P = 0.024). The lowest triglyceride levels were found in the normal group of 96.50 mg/dL, followed by the standard group of 102.00 mg/dL, the turmeric ethanol extract group (Curcuma Longa) I, II, III, and the group with the highest triglyceride levels was the control group of 166.50 mg/dL.
c. LDL levels also showed significant differences across the treatment group, this can be seen from the value of P < 0.05. The lowest average LDL levels were found in the normal group of 52.00 ± 1.60 mg/dL, followed by the standard group of 62.00 ±1.20 mg/dL, the turmeric ethanol extract group (Curcuma Longa) I, II, III, and the group with the highest LDL levels was the control group of 106.20 ±3.50 mg/dL.
d. HDL levels also showed significant differences across the treatment group, this can be seen from the value of P < 0.05 (Value P = 0.024). The highest hdl levels were found in

the normal group of 60.00 mg/dL, followed by the standard group of 59.50 mg/dL, the Turmeric extract group (Curcuma Longa)I, II, III, and the group with the lowest HDL levels was the control group of 27.00 mg/dL.

Another parameter that was also assessed in the entire group of mice at the end of the study was liver function, namely: SGOT and SGPT levels. Comparison of SGOT and SGPT levels in the entire group of rat treatment can be seen in the table below.

Table 8. Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Group	SGOT rate (U/L)	SGPT rate (U/L)
Normal	26.00 (25-29)[a]	45.50 ± 1.50[a]
Standard	110.00 (104-110)[b]	169.00 ± 1.20[b]
Control	165.00 (160-170)[c]	96.25 ± 1.50[c]
Turmeric Ethanol Extract (Curcuma Longa) I	116.00 (116-120)[d]	100.50 ± 3.50[d]
Turmeric Ethanol Extract (Curcuma Longa) II	120.50 (119-120)[e]	114.00 ± 4.50[e]
Turmeric Ethanol Extract (Curcuma Longa) III	128.00 (126-130)[f]	140.00 ± 2.00[b]
P Value	**0.024**	**< 0.05**

From the table data above, it was seen that SGOT and SGPT levels in the entire rat treatment group showed significant differences, this is seen from the value of $P < 0.05$. The tendency of the highest SGOT levels was found in the control group which was 165.00 U/ L and the lowest normal group was 26.00 U/ L. Meanwhile, a similar picture was found in the SGPT level, the group with the highest SGPT level was found in the standard group of 169.00 U/ L and the low was 45.50 U/ L.

4.2 Discussion

The most common fat in the diet is neutral fat, known as trialyglycerol. Neutral fats are the main ingredients in animal-derived foodstuffs and are very little present in plant-derived foods. According to Harsa (2014), in his research entitled The Effect of Giving a High Fat Diet to the Blood Fat Profile of White Rats (Rattus norvegicus). Where the results showed that the group who were given a high-fat diet for 4 weeks experienced an increase in average levels of total cholesterol of 87.17 mg / dL compared to the group who were only given a standard diet for 4 weeks with an average total cholesterol level of 57.33 mg / dL these results showed there had been hypercholeerolemia. With the conclusion of research with the administration of a high-fat diet can increase levels of total cholesterol, LDL cholesterol, triaglyceride and reduce HDL cholesterol levels significantly in the blood of white mice (Rattus norvegicus) (Harsa, 2014).

The most common fat in the diet is neutral fat, known as trialyglycerol. Neutral fats are the main ingredients in animal-derived foodstuffs and are very little present in plant-derived foods. According to Harsa (2014), in his research entitled The Effect of Giving a High Fat Diet To the Blood Fat Profile of White Rats (Rattus norvegicus). Where the results showed that the group who were given a high-fat diet for 4 weeks experienced an increase in average levels of total cholesterol of 87.17 mg / dL compared to the group who were only given a standard diet for 4 weeks with an average total cholesterol level of 57.33 mg / dL these results showed there had been hypercholeerolemia. With the conclusion of research with

the administration of a high-fat diet can increase levels of total cholesterol, LDL cholesterol, triaglyceride and reduce HDL cholesterol levels significantly in the blood of white mice (Rattus norvegicus).

The anti-dislipidemia effects of turmeric ethanol extract (Curcuma Longa) can be related to the content of various phytochemicals in turmeric rhizomes. Several studies have shown the potential of phytochemicals as anti-dyslipidemia. Polyphenol content can cause down-regulation of pro-inflammatory cell signal modulation such as nuclear factor-ϰB, activated protein-1, and mitogen activated protein kinase through the inhibition of the arachidonic acid cascade and eicosanoids derivates. Another mechanism that allows the anti-dyslipidemia effects of polyphenol compounds is the regulation of intestinal mirkobiota. Polyphenol compounds in the usu will interact with the gut microbiota thus increasing various beneficial metabolite products such as short-chain free fatty acids, in addition to usu microbes such as Akkermansia municiphilia sp. Restore inflammatory conditions in the intestines, improve intestinal permeability, and inslin sensitivity. Furthermore, this improvement to the gut microbiota protects the gut-liver axis thereby lowering lipid profiles in the body (Sun, Wang and Qin, 2018; Feldman *et al.*, 2021)

Other studies discussing the anti-dislipidemia effects of turmeric ethanol are still limited, but the results of Ardhani's study (2017), entitled Effectiveness of Turmeric Extract (Curcuma domestica) as a Non-Pharmacological Therapy Dislipidemia and Antiatherosklerosis, stated that the administration of turmeric extract can be a non-pharmacological therapy dislipidemia and as an antiatherosclerosis substance. Turmeric extract contains curcumin compounds which are antioxidants. Curcumin can decrease LDL oxidation which plays a role in the formation of foam cells, suppress inflammatory processes in blood vessels, and protect the endothelial blood vessels from free radicals (Ardhani *et al.*, 2017). In addition to being an antioxidant, curcumin can lower cholesterol levels due to inhibiting the reabsorbtion of cholesterol from the outside (exogenous) and increase the enzyme Hmg-CoA reductase inhibitor so that fat synthesis can run properly (Komang and Laksmi, 2014). Treatment and prevention of diseases 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 lowered SGOT and SGPT levels compared to the control group. This decrease in SGOT and SGPT levels is associated with improvement of Non-Alcoholic Fatty Liver Disease (NAFLD). Several studies have shown that NAFLD is a risk factor for arterosclerosis. This is because NAFLD causes dysfunction of the endothelial blood vessels. Thong and Quynh (2021) report that both SGOT and SGPT correlate with the occurrence of NAFLD, but the use of SGOT and SGPT separately can indicate errors in confirming mild NAFLD. In the case of severe NAFLD, SGOT will increase slightly and in milder cases SGOT levels can be found in normal amounts. Therefore, the use of SGOT and SGPT unilaterally may allow errors in confirming mild degree NAFLD (Thong and Quynh, 2021).

In this study, SGOT and SGPT levels in the group of mice that received turmeric ethanol extract (Curcuma Longa) were lower than the SGOT and SGPT levels of the control group. This suggests that turmeric ethanol extract (Curcuma Longa) may protect liver tissue from NAFLD compared to the group that didn't get turmeric ethanol (Curcuma Longa). However, the possibility of mild naFLD degrees in the group of rats that get turmeric ethanol (Curcuma Longa) cannot be removed.

V. Conclusion

The conclusion that can be drawn from the results of this study is that turmeric ethanol extract (Curcuma Longa) III (150.20 ± 0.90 mg / dl) can significantly reduce total cholesterol compared to the control group (177.50 ± 6.02mg / 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 (166.50 (160-175) mg/dl), (value P = 0.024). Turmeric ethanol extract (Curcuma Longa) III (66.50 ± 1.25 mg/dl) significantly lowered LDL levels compared to the control group (106.20 ± 3.50 mg/dl), (P value < 0.05). Turmeric ethanol extract (Curcuma Longa) III, (60.00 (59-61) mg/dl) can significantly increase HDL levels compared to the control group (27.00 (33-39) mg/dl), (Value P = 0.024). Turmeric ethanol extract (Curcuma Longa) III significantly lowered SGOT (Value = 0.024) and SGPT (Value P < 0.05) compared to the control group.

References

Abarikwu, S. O. et al. (2020) 'Evaluation of the protective effects of quercetin and gallic acid against oxidative toxicity in rat's kidney and HEK-293 cells', Toxicology Reports, 7(February), pp. 955–962. doi: 10.1016/j.toxrep.2020.07.015.

Aldahmash, B. A. and El-Nagar, D. M. (2016) 'Antioxidant Effects of Captopril against Lead Acetate-Induced Hepatic and Splenic Tissue Toxicity in Swiss Albino Mice', Saudi Journal of Biological Sciences, 23(6), pp. 667–673. doi: 10.1016/j.sjbs.2016.05.005.

Aparicio, H. J. et al. (2021) Heart Disease and Stroke Statistics-2021 Update A Report from the American Heart Association, Circulation. doi: 10.1161/CIR.0000000000000950.

Ardhani, S. et al. (2017) 'Efektivitas Ekstrak Kunyit (Curcuma domestica) Sebagai Terapi Non Farmakologi Dislipidemia dan Antiaterosklerosis', Medula, 7(5), pp. 194–198.

Batubara, M. S., Sabri, E. and Tanjung, M. (2017) 'Pengaruh Pemberian Ekstrak Etanol Daun Andaliman (Zanthoxylum acanthopodium DC.) terhadap Gambaran Morfologi Ovarium Mencit (Mus musculus L.) Strain DDW', Klorofil, 1(1), pp. 5–10.

D'Agostino, R. B. et al. (2008) 'General cardiovascular risk profile for use in primary care: The Framingham heart study', Circulation, 117(6), pp. 743–753. doi: 10.1161/CIRCULATIONAHA.107.699579.

Dipiro J et al. (2015) Pharmacoterapy A Phatophysiologic Approach, AIAA Guidance, Navigation, and Control Conference.

El-Sayed, E. M. et al. (2011) 'Cardioprotective effects of Curcuma longa L. extracts against doxorubicin-induced cardiotoxicity in rats', Journal of Medicinal Plants Research, 5(17), pp. 4049–4058.

Feldman, F. et al. (2021) 'Efficacy of polyphenols in the management of dyslipidemia: A focus on clinical studies', Nutrients, 13(2), pp. 1–42. doi: 10.3390/nu13020672.

Fouad, A. A. and Jresat, I. (2013) 'Captopril and telmisartan treatments attenuate cadmium-induced testicular toxicity in rats', Fundamental and Clinical Pharmacology, 27(2), pp. 152–160. doi: 10.1111/j.1472-8206.2011.00974.x.

Ge, Y. et al. (2018) 'Adipose-derived stem cells alleviate liver apoptosis induced by ischemia-reperfusion and laparoscopic hepatectomy in swine', Scientific Reports, 8(1), pp. 1–11. doi: 10.1038/s41598-018-34939-x.

Gustomi Rima, M. P. L. (2015) 'Ekstrak Rimpang Kunyit Menurunkan Kadar Lemak Darah Pasien Hiperlipidemia (Turmeric (Curcuma Longa Linn) Extract toward Modification of Blood Lipid Level in Hyperlipidemia Patients)', Journals of Ners Community, 6(Vol 6, No 1 (2015)), pp. 1–7. Available at: http://journal.unigres.ac.id/index.php/JNC/article/view/66.

Harsa, I. M. S. (2014) 'Efek Pemberian Diet Tinggi Lemak Terhadap Profil Lemak Darah Tikus Putih (Rattus norvegicus)', Universitas Wijaya Kusuma, 31(1), pp. 21–28.

Hartati, S. Y. (2013) 'Perkebunan_KhasiatKunyit.pdf', Warta Penelitian dan Pengembangan Tanaman Industri, p. 5. Available at: https://perkebunan.litbang.pertanian.go.id/wp-content/uploads/2014/02/Perkebunan_KhasiatKunyit.pdf.

Jijith, U. S. and Jayakumari, S. (2018) 'Screening methods for antihyperlipidemic activity : A review', 10(2), pp. 2017–2019.

Kemenkes RI (2018) 'Hasil Riset Kesehatan Dasar Tahun 2018', Kementrian Kesehatan RI, 53(9), pp. 1689–1699.

Kocaadam, B. and Şanlier, N. (2017) 'Curcumin, an active component of turmeric (Curcuma longa), and its effects on health', Critical Reviews in Food Science and Nutrition, 57(13), pp. 2889–2895. doi: 10.1080/10408398.2015.1077195.

Komang, N. and Laksmi, S. (2014) 'Continuing Continuing Development Professional Medical Development', 41(11), pp. 823–827.

Kosasih, E. et al. (2019) 'Hepatoprotective Effect of Citrus Sinensis Peel Extract Against Isoniazid and Rifampicin-induced Liver Injury in Wistar Rats', Majalah Obat Tradisional, 24(3), pp. 197–203. doi: 10.22146/mot.45762.

Manarin, G. et al. (2019) 'Curcuma longa L. ameliorates asthma control in children and adolescents: A randomized, double-blind, controlled trial', Journal of Ethnopharmacology, 238, p. 111882. doi: 10.1016/j.jep.2019.111882.

Mawarti, H., Ratnawati, R. and Lyrawati, D. (2012) 'Epigallocatechin Gallate Menghambat Resistensi Insulin pada Tikus dengan Diet Tinggi Lemak Inhibitory Effect of Epigallocatechin Gallate on Insulin Resistance in Rat with High Fat Diet', Jurnal Kedokteran Brawijaya, 27(1), pp. 43–50.

Mutia, M. S. and Chiuman, L. (2019) 'Hepatoprotective Effect of Citrus sinensis (L .) Osbeck Ethanol Extract in Paracetamol-Induced Rats Efek Hepatoprotektif Ekstrak Etanol Citrus sinensis L . Osbeck pada Tikus yang Diinduksi Parasetamol', Majalah Kedokteran Bandung, 51(4), pp. 189–193.

Nabofa, W. E. E. et al. (2018) 'Cardioprotective Effects of Curcumin-Nisin Based Poly Lactic Acid Nanoparticle on Myocardial Infarction in Guinea Pigs', Scientific Reports, 8(1), pp. 1–11. doi: 10.1038/s41598-018-35145-5.

Olayinka, E. T. et al. (2014) 'Protective effect of quercetin on melphalan-induced oxidative stress and impaired renal and hepatic functions in rat', Chemotherapy Research and Practice, 2014. doi: 10.1155/2014/936526.

Razavi, et al (2021) 'A review of therapeutic potentials of turmeric (Curcuma longa) and its active constituent, curcumin, on inflammatory disorders, pain, and their related patents', Phytotherapy Research, (July), pp. 1–25. doi: 10.1002/ptr.7224.

Rezzani, R., Franco, C. and Rodella, L. F. (2019) 'Curcumin as a therapeutic strategy in liver diseases', Nutrients, 11(10), pp. 1–7. doi: 10.3390/nu11102498.

Sabale, P., Modi, A. and Sabale, V. (2013) 'Curcuma longa Linn. A Phytochemical and Phytopharmacological Review', Research Journal of Pharmacognosy and Phytochemistry, 5(2), pp. 59–68.

Setiadi, A., Khumaida, N. and Wahyuning Ardie, D. S. (2017) 'Keragaman Beberapa Aksesi Temu Hitam (Curcuma aeruginosa Roxb.) Berdasarkan Karakter Morfologi', Jurnal Agronomi Indonesia (Indonesian Journal of Agronomy), 45(1), pp. 71–78. doi: 10.24831/jai.v45i1.13773.

Shishodia, S. et al. (2005) 'Curcumin (diferuloylmethane) inhibits constitutive NF-κB activation, induces G1/S arrest, suppresses proliferation, and induces apoptosis in mantle cell lymphoma', Biochemical Pharmacology, 70(5), pp. 700–713. doi: 10.1016/j.bcp.2005.04.043.

Sun, Y. E., Wang, W. and Qin, J. (2018) 'Anti-hyperlipidemia of garlic by reducing the level of total cholesterol and low-density lipoprotein', Medicine (United States), 97(18), pp. 1–8. doi: 10.1097/MD.0000000000010255.

Thong, V. D. and Quynh, B. T. H. (2021) 'Correlation of serum transaminase levels with liver fibrosis assessed by transient elastography in vietnamese patients with nonalcoholic fatty liver disease', International Journal of General Medicine, 14, pp. 1349–1355. doi: 10.2147/IJGM.S309311.

Untari, M. K. and Pramukantoro, G. E. (2020) 'Aktivitas Antihiperkolesterolemia Ekstrak Etanol Daun Stevia Rebaudiana Bertoni Pada Tikus Putih Jantan', Journal Syifa Sciences and Clinical Research, 2(1), pp. 11–20. doi: 10.37311/jsscr.v2i1.2700.

Wanninger, S. et al. (2015) 'Metal complexes of curcumin - synthetic strategies, structures and medicinal applications', Chemical Society Reviews, 44(15), pp. 4986–5002. doi: 10.1039/c5cs00088b.

Widowati, W. et al. (2016) 'Antioxidant and Anti Aging Assays of Oryza sativa Extracts, Vanillin and Coumaric Acid', Journal of Natural Remedies, 16(3), pp. 88–99. doi: 10.18311/jnr/2016/7220.

Widowati, W. et al. (2017) 'Antioxidant and antiaging assays of Hibiscus sabdariffa extract and its compounds', Natural Product Sciences, 23(3), pp. 192–200. doi: 10.20307/nps.2017.23.3.192.

Widowati, W. et al. (2018) 'Antioxidant and antiaging activities of Jasminum sambac extract, and its compounds', Journal of Reports in Pharmaceutical Sciences, 7(3), pp. 270–285.

Worotikan, R. V., Tuju, E. A. and Kawuwung, F. (2017) 'Analisa Efektivitas Antidiabetes Ekstrak Etanol Buah Andaliman (Zanthoxylum acanthopodium DC) pada Histopatologi Ginjal Tikus Putih (Rattus norvergicus) yang Diinduksi Alloksan', Jurnal Sains Matematika & Edukasi, 5(1), pp. 29--37.

Wulansari, F. (2020) 'Aktivitas Water Kefir sebagai Antidislipidemia pada Tikus Putih Jantan yang Diinduksi Propylthiouracil (PTU) dan Emulsi Lemak', Universitas Bhakti Kencana Fakultas Farmasi Program Strata I Farmasi Bandung 2020, Laporan Tu, pp. 5–24.

Yunarto, N. et al. (2019) 'Aktivitas Antioksidan serta Penghambatan HMG CoA dan Lipase Kombinasi Ekstrak Daun Binahong-Rimpang Temulawak Antioxidant Activity along with Inhibition of HMG CoA Reductase and Lipase from Anredera cordifolia Leaf - Curcuma xanthorrhiza Rhizome Combinati', 9(2), pp. 89–96.