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Analysis Of Anti Dislipidemia Effects of Etanol Extract of Kunyit (Curcuma Longa) On Propylthiouracil-Fed Wistar Rats

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ABSTRACT
One of the main risk factors for atherosclerosis is dyslipidemia; in Indonesia, the prevalence of dyslipidemia is increasing. The number of people with heart disease in Indonesia reached 1.017 million, while stroke patients reached 713,783 in 2018. This study aimed to determine the effectiveness of turmeric ethanol extract (Curcuma Longa) as anti-dyslipidemia in male Wistar rats given Propylthiouracil (PTU). This study is experimental 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 using the Federer formula so that four rats were assigned to each treatment. The results of turmeric ethanol extract can significantly reduce total cholesterol and triglyceride levels compared to the control group (P value = 0.019). Turmeric ethanol extract can significantly increase HDL levels (P value = 0.027). Turmeric ethanol extract can dramatically reduce SGOT (P value = 0.019) and SGPT (P value < 0.05) levels compared to the control group.
Keywords: *Curcuma Longa, Dyslipidemia, propylthiouracil.*

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I. Introduction

One of the main risk factors for atherosclerosis is dyslipidemia; in Indonesia, the prevalence of dyslipidemia is increasing. MONICA study in Jakarta 1988 showed that the average level of total cholesterol in women was 206.6 mg/dl and men 199.8 mg/dl; in 1993, it increased to 213.0 mg/dl in women and 204.8 mg/dl in men. In some areas, the same cholesterol values are Surabaya (1985): 195 mg/dl, Ujung Pandang (1990): 219 mg/dl, and Malang (1994): 206 mg/dl. (1). The number of heart disease patients in Indonesia reached 1.017 million, while stroke patients reached 713,783 in 2018 (2). Based on estimates from the AHA, 42.8% or 100,100,000 million American adults over the age of 20 have total cholesterol levels of 200 mg/dL (5.17 mmol/L) or higher (3). According to Jeppsen et al., the higher the level of triglycerides in the blood of an individual, the higher the risk of developing cardiovascular disease in that individual (4).

Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in lipid fractions in plasma. The most crucial lipid fraction abnormalities are an increase in total cholesterol, LDL cholesterol, an increase in triglyceride levels, and a decrease in HDL levels. In the process of atherosclerosis, all of them have an essential role and are closely related to one another, so it is impossible to discuss them individually. The three are also known as the Lipid Triad (5). The primary lipid fraction abnormalities are an increase in total cholesterol, LDL (Low-Density Lipoprotein) cholesterol, triglycerides, and a decrease in HDL (High-Density Lipoprotein) cholesterol (3) (6). The disease is also one of the risk factors for atherosclerosis, which can cause Coronary Heart Disease (CHD) (7).

Using drugs made from natural ingredients also tends to be safer than chemical drugs (Haryana, 2007). One of these wild plants is turmeric, which contains the main compound of curcumin (Ariani, 2017). Besides being an antioxidant, curcumin can reduce cholesterol levels by inhibiting the reabsorption of cholesterol from outside (exogenous) and increasing the enzyme HMG-CoA reductase inhibitor so that fat synthesis can run well (8). The function of curcumin has been proven in a study of dyslipidemia patients in the Sawotratap village area of Sidoarjo Regency who were given turmeric extract for 12 days. Cholesterol levels were measured before and after the administration of turmeric rhizome extract. Based on the results of the study obtained with the Paired t-test analysis test, it was stated that there was a significant difference in changes in blood lipid levels in research respondents (9). This study aimed to determine the effectiveness of turmeric ethanol extract (Curcuma Longa) as anti-dyslipidemia in male Wistar rats given Propylthiouracil (PTU).

II. 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 using the Federer formula:

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

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

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

Based on the results of these calculations, it can be concluded that at least four male Wistar rats (Rattus norvegicus) are needed in each treatment group. Rat body weight ranges from 180-200 grams, and ages between 2-4 months.

The phytochemical test study uses a modified Farnsworth method, identifying phenols, steroids/triterpenoids, terpenoids, saponins, flavonoids, tannins, and alkaloids (10–12).

Table 1. Treatment Overview of Each Group

No	Test Group	Treatment
1.	Normal	Test animals were not given specific treatment, only food and drink ad libitium.
2.	Control	Test animals were given 1 ml of 0.5% Na CMC suspension daily for 14 days. Food and drink were provided ad libitum.
3.	Standard (25 mg/kg body weight)	The test animals were given an oral suspension of simvastatin 5 ml/ kg body weight daily for 14 days. Food and drink were provided ad libitum.
4.	Turmeric Extract *(Curcuma Longa)* - I (500 mg/ kg body weight)	Test animals were given Turmeric Extract (Curcuma Longa) at a dose of 5 ml / kg body weight daily for 14 days. Food and drink were provided ad libitum.
5.	Turmeric Extract *(Curcuma Longa)* - II (1000 mg/kg body weight)	Test animals were given Turmeric Extract (Curcuma Longa) at 10 ml / kg body weight daily for 14 days. Food and drink were provided ad libitum.
6.	Turmeric Extract *(Curcuma Longa)* - III (1500 mg/kg body weight)	Test animals were given Turmeric Extract (Curcuma Longa) at a dose of 15ml / kg body weight daily for 14 days. Food and drink are provided ad libitum.

The research data were then analyzed using the SPSS 25 program. The research data were analyzed descriptively (Central tendency and Dispersion) from the data in lipid profiles (LDL, HDL, Total Cholesterol, and Triglycerides), color, texture, and weight. Then, the research data in the form of lipid profiles were analyzed with One-Way Anova if the data were normally distributed with further tests in the form of Post Hoc Tukey HSD tests to see fundamental differences between treatments. However, if the data is not normally distributed, the Kruskall-Wallis test is used as an alternative test.

III. Research Results

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

Treatment Group	Total cholesterol (mg/dL)	
	Before Induction	**After Induction**
Normal	116.00 (110-115)	117.50 (111-122)[b]
Standard	113.00 (110-117)	211.00 (209-211)[a]
Control	116.50 (110-115)	210.00 (210-212)[b]
Turmeric Extract *(Curcuma Longa)* -I	116.00 (110-115)	210.50 (208-214)[b]
Turmeric Extract *(Curcuma Longa)*-II	112.50 (100-110)	210.00 (209-212)[b]
Turmeric Extract *(Curcuma Longa)*-III	117.00 (117-125)	210.50 (208-212)[b]
P-value	**0.783**	**0.032**

Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; different superscripts in the same column indicate significant differences.

From the data table above, it can be seen that before being given a high-fat diet, the total cholesterol of rats before giving a high-fat diet in all treatment groups did not show significant differences (P value = 0.783). This indicates that the entire cholesterol data of rats before being given a high-fat diet is uniform. However, the total cholesterol in all groups of rats after the high-fat diet showed a different distribution, where only the control, standard, turmeric extract (Curcuma longa)-I, II, and III groups showed uniform total cholesterol.

Table 3. Comparison of Lipid Profile in All Rat Treatment Groups

Treatment Group	Profil Lipid			
	Total cholesterol *	**Trigliserida****	**LDL***	**HDL****
Normal	146.00 ± 2.40a	98.50 (97-100)a	52.70 ± 1.64a	62.50 (61-64)a
Standard	147.50 ± 0.58b	102.00 (101-105)b	63.00 ±1.27b	60.50 (60-63)a
Control	172.00 ± 6.05c	186.00 (162-179)c	105.30 ±3.20c	27.00 (37-22)b
Turmeric Extract *(Curcuma Longa)*-I	167.25 ± 1.50d	133.50 (133-135)d	83.75 ±2.62d	57.50 (56-59)b
Turmeric Extract *(Curcuma Longa)*-II	163.25 ± 2.36e	120.50 (119-122)e	77.50 ± 1.29e	61.50 (61-63)a
Turmeric Extract *(Curcuma Longa)* -III	151.70 ± 0.92e	110.00 (102-112)f	68.50 ±1.28f	61.00 (62-62)a
P-value	**< 0.05**	**0.019**	**< 0.05**	**0.019**

* Data are shown as Mean ± SD. P values obtained from One Way ANOVA analysis; **Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; Different superscript in the same column indicates significant difference..

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

a. aTotal cholesterol in all rat treatment groups showed significant differences; this can be seen from the P value <0.05. The lowest mean total cholesterol was found in the standard group at 146.00 ± 2.40 mg/dL, followed by the legal group at 147.50 ± 0.58 mg/dL, the turmeric ethanol extract group (Curcuma Longa) I, II, III, and the group with the highest total cholesterol was the control group at 172.00 ± 6.02 mg/dL;

b. bTriglyceride levels in all treatment groups also showed significant differences; this can be seen from the P value <0.05 (P value = 0.019). The trend of the lowest triglyceride levels was found in the standard group at 98.50 mg/dL, followed by the legal group at 102.00 mg/dL, Turmeric (Curcuma Longa) ethanol extract groups I, II, III, and the group with the highest triglyceride levels was the control group at 186.00 mg/dL.

c. cLDL levels also showed significant differences in all treatment groups; this can be seen from the value of P < 0.05. The lowest average LDL level was found in the standard group at 52.70 ± 1.64 mg/dL, followed by the legal group at 63.00 ± 1.27 mg/dL, the turmeric ethanol extract group (Curcuma Longa) I, II, III, and the group with the highest LDL level was the control group at 105.30 ± 3.20 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 = 0.019). The trend of the highest HDL levels was found in the standard group, which was 62.50 mg/dL, followed by the usual group of 60.50 mg/dL, Turmeric (Curcuma Longa) extract group I, II, III, and the group with the lowest HDL levels was the control group of 27.00 mg/dL.

Table 4. Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Group	SGOT levels (U/L)	SGPT levels (U/L)
Normal	28.50 (27-30)^{a}	46.00 ± 1.50^{a}
Standard	110.00 (106-110)^{b}	162.00 ± 2.21^{b}
Control	178.20 (162-170)^{c}	97.25 ± 1.50^{c}
Turmeric Extract *(Curcuma Longa)* -I	117.50 (116-120)^{d}	100.75 ± 3.56^{d}
Turmeric Extract *(Curcuma Longa)*-II	121.00 (120-124)^{e}	115.00 ± 4.50^{e}
Turmeric Extract *(Curcuma Longa)*-III	129.50 (128-130)^{f}	142.00 ± 2.08^{b}
P-value	**0.019**	**< 0.05**

*Data are shown as Mean ± SD. P values obtained from One Way ANOVA analysis; **Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; Different superscript in the same column indicates significant difference.

From the data table above, it can be seen that the SGOT and SGPT levels in all rat treatment groups show significant differences; this can be seen from the P value <0.05. The trend of the highest SGOT level was found in the control group, 178.20 U/L, and the lowest in the standard group, 27.50 U/L. Meanwhile, a similar picture was found in the SGPT level; the group with the highest SGPT level was found in the traditional group, 162.00 U/L, and the lowest was found in the standard group, 46.00 U/L.

IV. Discussion

Turmeric is a species of Curcuma domestica Val (Winarto, 2004), a traditional medicinal plant (jamu) in Indonesia. The main chemical compounds contained in turmeric are curcuminoids or dyes, which are as much as 2.5 - 6%. Chemical components contained in turmeric rhizomes include essential oils, starch, bitter substances, resins, cellulose, and some minerals. The content of turmeric essential oil is about 3 - 5% (Winarto, 2004). Turmeric has pharmacological effects such as smoothing blood and vital energy, removing menstrual obstruction, anti-inflammatory, facilitating labor, antibacterial, facilitating bile secretion (cholagogue), carminative and moisturizing (astringent (14): (15); (16); (17). Dyslipidemia is 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-dyslipidemia activity, namely in vivo and in vitro methods (18,19). Vivo methods include Triton, PTU, and High Fat Diet-

induced dyslipidemic rat models. In Vitro method with Caco-2 cells or measurement of HMG-CoA Reductase enzyme inhibition activity.

This study showed that turmeric ethanol extract (Curcuma Longa) showed significant lipid profile improvement at the end of the study. At the highest dose, ethanol turmeric (Curcuma Longa) showed the most optimal lipid profile improvement. This can be seen from the decrease in total cholesterol, triglyceride, and LDL levels and the increase in HDL levels of the turmeric ethanol (Curcuma Longa)-II and III groups. However, these improvements in lipid profiles in the Turmeric (Curcuma Longa)-III ethanol group of rats did not exceed the gains shown in the standard group. The anti-dyslipidemia effect possessed by the ethanol extract of Turmeric (Curcuma Longa) can be related to the content of various phytochemicals in turmeric rhizomes.

According to Ardhani (2017), the administration of turmeric extract can be a non-pharmacological therapy for dyslipidemia and as an antiatherosclerotic substance. Turmeric extract contains curcumin compounds, which are antioxidants. Curcumin can reduce LDL oxidation, which plays a role in foam cell formation, suppresses the inflammatory process in blood vessels, and protects the vascular endothelium from free radicals (6). Besides being an antioxidant, curcumin can reduce cholesterol levels by inhibiting the reabsorption of cholesterol from outside (exogenous) and increasing the enzyme Hmg-CoA reductase inhibitor so that fat synthesis can run well (20). Treatment and prevention of diseases with curcumin is one of the therapeutic modalities that is not inferior to pharmacological approaches (21). Turmeric ethanol extract also significantly reduced SGOT and SGPT levels compared to the control group. This decrease in SGOT and SGPT levels is associated with improved Non-Alcoholic Fatty Liver Disease (NAFLD). Several studies have shown that NAFLD is a risk factor for the development of arteriosclerosis (22).

V. Conclusion

The conclusions that can be drawn from the results of this study are as follows:

a. Turmeric ethanol extract can significantly reduce total cholesterol and triglyceride levels compared to the control group (P value = 0.019)

b. Turmeric ethanol extract can significantly increase HDL levels (P value = 0.027)

c. Turmeric ethanol extract can significantly reduce SGOT (P value = 0.019) and SGPT (P value <0.05) levels compared to the control group.

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