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Antidyslipidemic Activity of *Curcuma xanthorrhiza* Rhizome Ethanol Extract on Low-Density Lipoprotein (LDL) and High-Density Lipoprotein (HDL) Levels in Male Wistar Rats

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ABSTRAK

Dislipidemia merupakan suatu kelainan metabolism lipid yang ditandai dengan peningkatan maupun penurunan kadar fraksi lipid dalam plasma. Rimpang temulawak mengandung senyawa flavonoid, fenol serta kurkumin yang berperan sebagai antioksidan. Aktivitas antioksidan xanthorrhizol murni dari temulawak dapat mengurangi peroksidasi LDL. Tujuan penelitian ini adalah untuk mengetahui aktivitas antidislipidemia dari ekstrak etanol rimpang *Curcuma xanthorrhiza* (EERC) terhadap kadar LDL dan HDL pada tikus Jantan galur wistar yang diinduksi pakan tinggi lemak. Tikus diberikan pakan tinggi lemak. Sebanyak 30 ekor tikus dibagi menjadi lima kelompok, setiap kelompok terdiri dari 6 tikus. Kelompok 1 (kontrol negatif) hewan uji dislipidemia dan diberikan larutan suspensi CMC-Na, kelompok 2 (kontrol positif) hewan uji dislipidemia dan diberikan suspensi simvastatin, kelompok 3, 4 dan 5 (perlakuan) hewan uji dislipidemia diberikan suspensi ekstrak etanol rimpang temulawak dengan dosis 400 mg/KgBB, 600 mg/KgBB dan 800 mg/KgBB. Pengukuran kadar HDL dan LDL dilakukan sebelum perlakuan (*pretest*) dan setelah perlakuan (*posttest*). Hasil analisis statistik antara data *pretest* dan *posttest* menunjukkan bahwa terjadi peningkatan kadar HDL yang signifikan pada pemberian dosis 600 mg/KgBB & dosis 800mg/KgBB ($p<0.001$) serta penurunan kadar LDL pada pemberian dosis 400 mg/KgBB, 600 mg/KgBB dan 800 mg/KgBB ($p<0.001$). Penurunan kadar LDL pada pemberian dosis 800 mg/KgBB memiliki efek yang setara dengan simvastatin sebagai kontrol positif (sig 0.057; $p>0.05$). Ekstrak etanol rimpang temulawak (*Curcuma xanthorrhiza*) memiliki aktivitas antidislipidemia pada tikus jantan galur wistar yang ditunjukkan dengan terjadinya peningkatan kadar HDL dan penurunan kadar LDL.

Kata Kunci: Temulawak, simvastatin, flavonoid, antidislipidemia

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ABSTRACT

Dyslipidemic is a lipid metabolism disorder characterized by an increase or decrease in plasma lipid fraction levels. Curcuma xanthorrhiza rhizome contains flavonoids, phenols, and curcumin, which act as antioxidants. The antioxidant activity of pure xanthorrhizol from Curcuma xanthorrhiza can reduce LDL peroxidation. The purpose of this study was to determine the antidyslipidemic activity of ethanol extract of Curcuma xanthorrhiza rhizome (EECR) on LDL and HDL levels in male wistar rats induced by a high-fat diet. Rats were fed a high-fat diet (HFD). 30 rats were divided into five groups, with each group consisting of 6 rats. Group 1 (negative control) dyslipidemia rats and given CMC-Na suspension, group 2 (positive control) dyslipidemia rats and given simvastatin suspension, group 3, 4 and 5 (treatment) dyslipidemia rats given EECR with doses of 400 mg/kg.b.w, 600 mg/kg.b.w and 800 mg/kg.b.w. Measurement of HDL and LDL levels was carried out before treatment (pretest) and after treatment (posttest). The results of statistical analysis between pretest and posttest data showed that there was a significant increase in HDL levels at doses of 600 mg/kg.b.w & 800mg/kg.b.w ($p < 0.001$) and a decrease in LDL levels at doses of 400 mg/kg.b.w, 600 mg/kg.b.w and 800 mg/kg.b.w ($p < 0.001$). The decrease in LDL levels at a dose of 800 mg/kg.b.w had an effect equivalent to simvastatin as a positive control (sig 0.057; $p > 0.05$). The ethanol extract of Curcuma xanthorrhiza rhizome has antidyslipidemic activity in male wistar rats which is indicated by an increase in HDL levels and a decrease in LDL levels.

Keywords: *Curcuma xanthorrhiza*, antidyslipidemic, flavonoid, simvastatin

INTRODUCTION

Hyperlipidemia is a metabolic disorder characterized by elevated plasma lipid levels, particularly total cholesterol, triglycerides, and low-density lipoprotein (LDL), accompanied by decreased high-density lipoprotein (HDL). Elevated LDL promotes cholesterol accumulation in artery walls and plaque formation, while HDL plays a protective role through reverse cholesterol transport, removing excess cholesterol from peripheral tissues to the liver. Therefore, maintaining a balance between LDL and HDL levels is crucial to prevent cardiovascular complications associated with dyslipidemia (Nelson, 2013; Ference *et al.*, 2017; Yusuf *et al.*, 2020; Pirillo *et al.*, 2021).

Pharmacological therapies such as statins are widely used to manage hyperlipidemia by inhibiting cholesterol synthesis in the liver. Although effective in lowering LDL levels and reducing cardiovascular risk, long-term statin use can cause side effects, including hepatotoxicity and muscle-related disorders. These

limitations have prompted the exploration of natural products as alternative therapeutic agents. Many medicinal plants contain bioactive compounds with antioxidant, anti-inflammatory, and lipid-lowering activities that may contribute to improved lipid metabolism and reduced cardiovascular risk (Endo, 2010; Patel *et al.*, 2012; Hegele *et al.*, 2014; Libby *et al.*, 2019)

C. xanthorrhiza Roxb. is a medicinal plant from the Zingiberaceae family, is widely used in traditional Indonesian medicine. Its rhizomes contain several bioactive compounds, including curcuminoids, xanthorrhizols, and essential oils, which exhibit antioxidant, hepatoprotective, and anti-inflammatory activities. These compounds have also been reported to influence lipid metabolism by inhibiting lipid peroxidation and modulating cholesterol biosynthesis and lipoprotein metabolism. (Hwang, Shim and Pyun, 2000; Devaraj *et al.*, 2014; Rahmani *et al.*, 2014; Oon *et al.*, 2015)

Several studies have reported the lipid-lowering potential of *C. xanthorrhiza* and related plants containing curcuminoids. Experimental studies in animal models of hyperlipidemia have shown that administration of curcumin or *C. xanthorrhiza* extract can reduce total and LDL cholesterol levels while increasing HDL concentrations. This effect is primarily attributed to the antioxidant properties of curcuminoids, which regulate lipid metabolism and reduce oxidative stress (Thiyagarajan and Sharma, 2004; Aggarwal and Harikumar, 2009; Panahi *et al.*, 2017).

Therefore, this study aimed to investigate the antidyslipidemic activity of ethanol extract of *C. xanthorrhiza* rhizome on LDL and HDL levels in male wistar rats. The results are expected to provide scientific evidence supporting the potential use of *Curcuma* as a natural therapeutic agent for managing hyperlipidemia.

MATERIALS AND METHODS

This study used an experimental pretest and posttest control design.

1. MATERIALS

Tools

The tools used in the study included an analytical balance, rotary evaporator, centrifuge, stirring rods and UV-Vis Spectrophotometer

Materials

The materials used in the study included ethanol extract of *C. xanthorrhiza* Roxb rhizome, ethanol, male wistar rats weighing 150-200 grams, simvastatin, NaOH, 1% CMC-Na, high-fat feed (egg yolk and beef brain in a 1:5 ratio), and filter paper.

2. METHOD

Preparation of Simvastatin Suspension

Ten simvastatin tablets were weighed individually, their average weight calculated, and then ground to a fine powder. The required amount of simvastatin powder was weighed, gradually added to a 1% w/v CMC-Na solution,and stirred until homogeneous. The homogeneous suspension was transferred to a 100 ml volumetric flask, which was then made up to 100 ml with a 1% w/v CMC-Na solution. The administered simvastatin dose was 10 mg (human dose), which was then converted to a dose of 0.9 mg/kg body weight for rats and concentration of 0.07 mg/mL.

Induction of Hyperlipidemia by High-Fat Diet (HFD)

Before treatment, all wistar male rats were acclimatized for three days. During the aclimatization period, they were provided with water and standard feed. 30 rats were divided into five groups, with each group consisting of 6 rats. Group 1 (negative control), Group 2 (positive control), and Groups 3, 4, and 5 (treatment). All wistar male rats were made dyslipidemic by giving high-fat diet (HFD). HFD induction consisting of chicken egg yolk and beef brain blended into a juice at a 1:5 (gram) ratio. HFD was administered orally twice daily in the morning and afternoon for 9 days (day 4 - 12).

Then blood samples were taken from all wistar male rats to measure HDL and LDL levels, and the results were recorded as pretest. In rats, the normal blood cholesterol level is 50–100 mg/dL. Therefore, the blood cholesterol level of rats with hypercholesterolemia is >100 mg/dL (BPOM, 2021)

Pharmacological Study Design

After blood samples were taken for pretest measurements of HDL and LDL levels, all wistar male rats were

replace with normal standard diet for the second 7 days of the treatment. Dyslipidemic rats were given treatment according to their respective groups, group 1 (negative control) dyslipidemic rats and given CMC-Na suspension solution; group 2 (positive control) dyslipidemic rats and given simvastatin suspension; group 3, 4 and 5 (treatment) dyslipidemic rats given ethanol extract of *C. xanthorrhiza* rhizome (EECR) with doses of 400 mg/kg.b.w, 600 mg/kg.b.w and 800 mg/kg.b.w. The vehicle, simvastatin solution or ethanol extract of *C. xanthorrhiza* were administered to the rats using a gastric force feeding needle, once daily for 7 days. Post-test HDL and LDL levels were measured after treatment was completed.

Statistical Analysis

The pretest and posttest HDL and LDL levels were then analyzed statistically by conducting normality and homogenity tests and one-way ANOVA with a 95% confidence level (a = 0.05).

RESULTS AND DISCUSSION

Prior to the study, research approval was obtained from Alma Ata University Ethics Committee Number: KE/AA/II/10112305/EC/2025. The research began by acclimatizing the wistar rats and weighed them. The purpose of acclimatization was to allow the rats to adjust to the new environmental conditions in the laboratory where the research would be conducted.

Table 1. HDL level Pretest and Posttest

Gr	*Pre-test (mg/dl)*	*Post-test (mg/dl)*	*p-Value (Paired Sample t-test)*	*Δ (mg/dl)*	*p-Value ANOVA*
1	18.5 ±3.7	42.3 ±6.1	0.001	23.8 ±8.2	0.561
2	19.4 ±2.5	39.1 ±1.3	0.000	19.7 ±1.3	
3	21.4 ±1.9	41.0 ±3.0	0.000	19.6 ±2.6	
4	18.5 ±1.5	40.9 ±2.2	0.000	22.4 ±0.9	
5	21.0 ±2.6	42.8 ±4.0	0.001	21.8 ±6.3	

Gr – Group; Δ – Changes; Gr 1 – Negative group; Gr 2 – Positive Group; Gr 3 – EECR 400 mg/kg.b.w Group; Gr 4 – EECR 600 mg/kg.b.w Group; Gr 5 – EECR 800 mg/kg.b.w Group; EECR (*ethanol extract of Curcuma xanthorrhiza rhizome*)

After the adaptation period, the all wistar male rats were induced with dyslipidemia by feeding them a HFD consisting of chicken egg yolk and beef brain blended into a juice at a 1:5 (gram) ratio. The beef brain was boiled then mixed with raw egg yolk and distilled water, then mashed until

evenly distributed (Masruroh, Nur and Restuti, 2023). 100 grams of beef brain contains approximately 2 grams of cholesterol and 2.9 grams of saturated fatty acids (Pratama and Probosari, 2012). Egg yolk contains 20 mg of cholesterol per gram. Approximately 95% of egg yolk cholesterol is found in triglyceride-rich lipoproteins (Widyaningsih, 2011).

HFD was administered orally twice daily—in the morning and afternoon—for 9 days (from day 4 to day 12). The HFD was administered only for 9 days because rats were already hypercholesterolemia. After *pretest* HFD was discontinued for all group. This is accordance with the study conducted to Sari *et. al* 2021 (Sari, Yuniastuti and Christijanti, 2021). HDL and LDL levels in all test animals were measured prior to the administration of treatments (pre-test). Treatments—EECR for the treatment group and simvastatin for the positive control group—were administered for 7 days. Post-treatment HDL and LDL levels were measured in all test animals (post-test).

An analysis of pre-test and post-test HDL and LDL values was conducted using a paired-sample t-test to determine whether there were significant differences between the pre-test and post-test levels. Comparisons of the increase in HDL values and the decrease in LDL levels between groups were analyzed using one-way ANOVA, followed by a post-hoc least significant difference (LSD) test.

Table 2. LDL level Pretest and Posttest

Gr	*Pre-test (mg/dl)*	*Post-test (mg/dl)*	*p-Value (Paired Sample t-test)*	*Δ (mg/dl)*	*p-Value ANOVA*
1	163.1 ±13.9	128.6 ±10.3	0.005	34.5 ±15.9	0.253
2	161.5 ±5.5	112.2 ±7.3	0.000	49.3 ±7.3	
3	170.9 ±7.5	124.1 ±5.2	0.000	46.8 ±10.2	
4	176.9 ±11.3	135.0 ±9.1	0.000	41.9 ±8.4	
5	169.7 ±7.5	122.2 ±6.6	0.000	47.5 ±11.6	

The study results showed an increase in HDL levels and a decrease in LDL levels following treatment across all groups. Paired-sample t-test analysis revealed significant differences in HDL and LDL values between pre-test and post-test measurements ($p < 0.05$). The mean increase in HDL levels (Δ) for groups 3, 4, and 5 was 19.6 ± 2.6 mg/dL, 22.4

± 0.9 mg/dL, and 21.8 ± 6.3 mg/dL, respectively, while increases of 23.8 ± 8.2 mg/dL and 19.7 ± 1.3 mg/dL were observed in group 1 (negative control) and group 2 (positive control) (Table 1). The mean decrease in LDL levels (Δ) for groups 3, 4, and 5 was 46.8 ± 10.2 mg/dL, 41.9 ± 8.4 mg/dL, and 47.5 ± 11.6 mg/dL, respectively, while decreases of 34.5 ± 15.9 mg/dL and 49.3 ± 7.3 mg/dL were observed in group 1 (negative control) and group 2 (positive control) (Table 2). Post-hoc LSD analysis demonstrated no significant differences in the increase of HDL (Table 4) or the decrease of LDL (Table 3) among the groups ($p > 0.05$).

Table 3. Significance values for the comparison of LDL reduction between groups using the LSD post-hoc test.

Gr	1	2	3	4	5
1					
2	0.046				
3	0.094	0,724			
4	0.304	0.305	0.497		
5	0.077	0.805	0.915	0.433	

Table 4. Significance values for the comparison of HDL reduction between groups using the LSD post-hoc test.

Gr	1	2	3	4	5
1					
2	0.178				
3	0.581	0.417			
4	0.537	0.454	0.948		
5	0.855	0.129	0.463	0.426	

Based on these results, it is evident that the effects of increasing HDL and decreasing LDL do not align linearly with increasing EECR dosages. The greatest increase in HDL was observed at a dosage of 600 mg/kg BW, whereas the most optimal reduction in LDL occurred at a dosage of 800 mg/kg BW. Increases in HDL and decreases in LDL were also observed in the negative control group. This phenomenon may be attributed to the discontinuation of the high-fat diet for all test animals, thereby triggering a spontaneous improvement in HDL and LDL levels

Ethanol extract of *Curcuma xanthorrhiza* Roxb rhizome contains flavonoids and alkaloids (Dewi, 2025). Flavonoids have the potential as antioxidants due to the hypothetical affinity series between flavonoids and amino acid residues, most of which provide significant applications regarding the prediction of interactions between flavonoids and

proteins in order to understand the biological activity of flavonoids (Ayu *et al.*, 2024). The mechanism of free radical prevention by flavonoids can be three, namely by slowing the formation of *Reactive Oxygen Species* (ROS), breaking down ROS and regulating or protecting with antioxidants (Alfaridz *et al.*, 2015)

CONCLUSIONS

Ethanol extract of *Curcuma xanthorrhiza* rhizome has antidyslipidemic activity in male wistar rats, which is indicated by an increase in HDL levels and a decrease in LDL levels.

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