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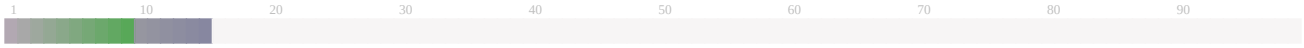

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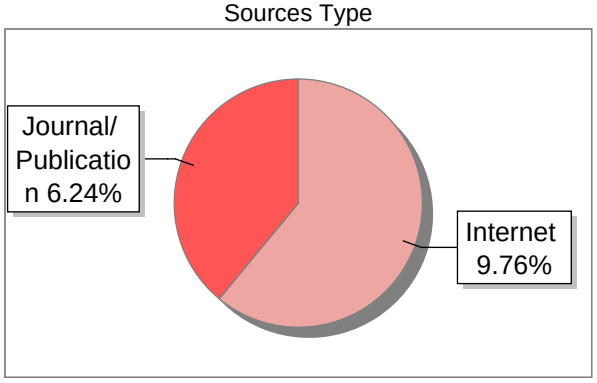

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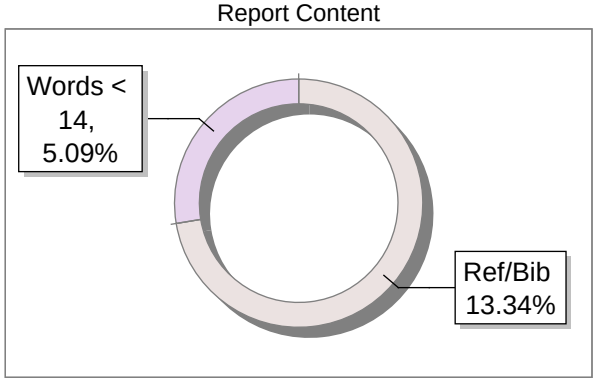

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Jurnal Farmasi dan Ilmu Kefarmasian Indonesia
Pharmacy and Pharmaceutical Sciences Journal
Published by Faculty of Pharmacy Universitas Airlangga
OPEN ACCESS
E-ISSN 2580-8303
P-ISSN 2406-9388

Jurnal Farmasi dan Ilmu Kefarmasian Indonesia Vol. 11 No. 1 April 2024, 61-70
DOI: 10.20473/jfiki.v11i12024.61-70
Available online at https://e-journal.unair.ac.id/JFIKI/

Jatropha curcas L. Leaf Extract Effects on Blood Pressure and Lipid Levels in Hypertensive Rats with High-Fat Diet

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Submitted: 17 November 2023
Revised: 16 Maret 2024
Accepted: 30 Maret 2024

Abstract

Background: *One of the main risk factors for cardiovascular diseases such as coronary atherosclerotic heart disease (CAHD) is dyslipidaemia or high levels of low-density lipoprotein (LDL) and triglycerides (TG) and low levels of high-density lipoprotein (HDL). Hypertension is also a cause of cardiovascular disease. One potential plant to lower LDL levels and blood pressure is Jatropha curcas, which is known to contain saponins, polyphenols, and flavonoids.* ***Objective***: *The purpose of this study was to determine the effect of the ethanol extract of Jatropha curcas leaves (EEJCL) on blood pressure, LDL levels, and HDL levels in hypertensive rats given a high-fat diet.* ***Methods***: *This study is an experimental study with a pretest-posttest control group design on male Wistar strain rats. Rats were divided into seven groups, namely the normal group, control group (induced with NaCl and given a high-fat diet), Captopril group, Simvastatin group, and EEJCL groups given doses of 1.8, 2.7, and 4.05 g/kg BW. The data obtained were analysed using the One-Sample Kolmogorov-Smirnov Test, Homogeneity of Variance, One-Way ANOVA, and Tukey Test.* ***Results***: *The results showed that the administration of EEJCL could significantly lower LDL levels and blood pressure and increase HDL levels ($p < 0.05$) at doses of 1.8, 2.7, and 4.05 g/kg BW, and the dose of 4.05 g/KgBW was the most optimal dose.* ***Conclusion***: *EEJCL has a potential for development in the treatment of hypertension and dyslipidaemia.*

Keywords: *blood pressure, cardiovascular, Jatropha curcas, HDL, LDL*

How to cite this article:
Bachri, M. S., Anita, W. Y., Lestari, P. D., Wulansari, D. E., Nengtyas, D. R., Ma'ruf, M., Yuliani, S., Widyaningsih, W., Nurani, L. H., Estiningsih, D., & Sofia, V. (2024). *Jatropha curcas* L. Leaf Extract Effects on Blood Pressure and Lipid Levels in Hypertensive Rats with High-Fat Diet. *Jurnal Farmasi dan Ilmu Kefarmasian Indonesia,* 11(1), 61-70. http://doi.org/10.20473/jfiki.v11i12024.61-70

P-ISSN: 2406-9388
E-ISSN: 2580-8303

INTRODUCTION

several other heart and blood vessel conditions, are the leading cause of global mortality and a major contributor to reduced quality of life. In 2017, CVDs caused around 17.8 million deaths worldwide, equivalent to 330 million years of life lost and 35.6 million more years lived with disability (Mensah *et al*., 2019).

Coronary atherosclerotic heart disease (CAHD) is characterized by dyslipidemia, manifesting as elevated levels of low-density lipoprotein (LDL) and triglycerides (TGs), alongside decreased levels of high-density lipoprotein (HDL). Elevated LDL levels can lead to plaque formation and inflammatory processes, resulting in the progression of atherosclerosis within arterial walls and thrombosis in CAHD. Meanwhile, HDL plays a protective role by reinforcing tissues surrounding arterial walls, inhibiting cholesterol deposition within arteries, and facilitating the repair of damaged endothelial membranes. Conversely, reduced levels of HDL impede the removal of cholesterol (Sun *et al*., 2022).

Evaluation of the lipid profile (triglycerides, LDL cholesterol, HDL cholesterol, and total cholesterol) in the blood is one way to identify the causes of hypertension, which is another cause of cardiovascular disease (Fuchs & Whelton, 2020). Research by Flint *et al*. (2019) on the influence of systolic and diastolic blood pressure on cardiovascular conditions explained that both systolic and diastolic blood pressure measuring ≥ 140/90 mm Hg and ≥130/80 mm Hg, respectively, significantly contribute to cardiovascular disease risk.

Hypertension, dyslipidemia, cardiovascular diseases (CVDs), and coronary atherosclerotic heart disease (CAHD) are interconnected conditions that can increase the risk of cardiovascular events. Dyslipidemia is a condition characterized by abnormal levels of lipids in the blood, and it is associated with an increased risk of hypertension. High levels of cholesterol can cause the blood vessels to become narrow and less elastic, leading to increased blood pressure (Hedayatnia *et al*., 2020).

Dyslipidemia is also a significant risk factor for CVDs, including CAHD. When dyslipidemia is present alongside hypertension, the risk of CVDs, including CAHD, increases. This is because both conditions contribute to the process of atherosclerosis, which is the buildup of plaque in the arteries. This plaque can lead to the narrowing and hardening of the blood vessels, reducing blood flow to the heart and increasing the risk of heart attack or stroke (Ariyanti and Besral, 2019). Futhermore, hypertension, dyslipidemia, CVDs, and CAHD are interconnected conditions that can increase the risk of cardiovascular events. Dyslipidemia is associated with an increased risk of hypertension and can exacerbate the risk of CVDs, including CAHD, when present alongside these conditions.

The prescriptions usually used for hypertension and dyslipidaemia are synthetic drugs such as Captopril and Simvastatin, but the use of herbal medicines is now developing and more preferred for long-term treatment due to their minimal side effects. One potential plant is *Jatropha curcas*, which is known to contain saponins, polyphenols, and flavonoids, that not only play a major role in treating various diseases, including bacterial and fungal infections, but also act as antioxidants (Ait Babahmad *et al*., 2018). According to Sadik *et al*. (2021), the administration of the ethanol extract of *Jatropha curcas* leaves can reduce blood pressure of hypertensive Wistar rats and can increase NO levels. In research conducted by Anita *et al*. (2023), it is reported that the administration of the ethanol extract of *Jatropha curcas* leaves can significantly reduce serum triglyceride levels at doses of 1.8, 2.7, and 4.05 g/kg BW. Research results on the effect of the ethanol extract of *Jatropha curcas* leaves on HDL and LDL levels have also been reported by Anigbogu (2015), revealing that the ethanol extract of *Jatropha curcas* leaves can increase HDL cholesterol concentration, thereby reducing LDL cholesterol concentration. This indicates that the ethanol extract of *Jatropha curcas* can be used for the treatment of cardiovascular diseases.

Due to the abundant presence of jatropha plants in Indonesia, numerous studies have examined the activity of the plants on blood pressure, LDL levels, and HDL levels. Therefore, the author intended to research the effect of giving the ethanol extract of *Jatropha curcas* leaves on blood pressure, LDL levels, and HDL levels in hypertensive rats given a high-fat diet.

MATERIALS AND METHODS

This study is an experimental study with a pretest-posttest control group design and has obtained ethical approval from Ahmad Dahlan University with the number 011804052. The test animals were grouped into seven groups, namely the normal group, negative control group, Captopril group, Simvastatin group, and EEJCL groups with doses of 1.8, 2.7, and 4.05 g/kg BW. The test animals in groups other than the normal group were induced with NaCl at 3.75 g/kg BW for 14 days to produce high blood pressure and a high-fat diet to produce hyperlipidaemia, while the normal group was only given standard feed.

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Materials

The materials used in this study were *Jatropha curcas* L. leaves obtained from the Gunung Kidul area of Yogyakarta and determined at the Biology Laboratory, Faculty of Applied Science and Technology, Ahmad Dahlan University, Yogyakarta, with the number 033/Lab.Bio/B/IV/2018, in addition to 96% ethanol, Captopril, Simvastatin, NaCl, Na-CMC, quercetin standard, gallic acid, Folin-Ciocalteau reagent, $AlCl_3$, Na_2CO_3, Silica gel 60 F_{254}, methanol, ethyl acetate, and chloroform. All the chemicals used were Merck chemicals of analytical grade. The test animals used were 35 male Wistar strain rats aged 2–3 months with weights of 200–250 grams.

Tools

The tools used included a drying cabinet, a blender, glassware, an analytical balance, a stirrer, a macerator, a vacuum, a rotary evaporator, water bath, a centrifuge, Eppendorf tubes, micropipettes, a vortex, and a UV-Vis spectrophotometer.

Methods

Preparation of the ethanol extract of *Jatropha curcas* Leaves (EEJCL)

As much as 1,700 grams of dried *Jatropha curcas* L. leaf powder was macerated using 96% ethanol as a solvent in a ratio of 1:4, stirred for 3 hours, and left to stand for 24 hours. Extraction was carried out 3 times. The extract was evaporated using a rotary evaporator at 70 °C and water bath until a thick extract was obtained (Anita & Bachri, 2023).

Compound identification using TLC

Thin layer chromatography (TLC) was carried out with silica gel F_{254} as the stationary phase, the mobile phase of hexane, ethyl acetate, and formic acid in the ratio of 6:4:0.2 for flavonoid analysis, and the mobile phase of HCl_3, MeOH, and H_2O in the ratio of 7:3.5:1. Sample spots were sprayed with $FeCl_3$ reagent for polyphenols and ammonia vapor for flavonoids and then compared to standard compound spots (quercetin serving as a flavonoid standard and gallic acid serving as a phenolic standard). The Rf value of each sample was determined (Susanto *et al*., 2023).

Total flavonoid test

The resulting sample with a concentration of 1% was pipetted at 2 mL and added with 2 mL of 2% $AlCl_3$. Absorbance was read with a spectrophotometer at a wavelength of 510 nm. The quercetin standard was prepared by dissolving quercetin in ethanol p.a at concentrations of 4, 6, 8, 10, and 12 µg/mL. The samples were examined with three replications. The flavonoid content was expressed as quercetin equivalent (Endah, 2016).

Total phenolic test

The resulting sample with a concentration of 1% was pipetted at 300 µL and added with 1.5 mL of Folin-Ciocalteu reagent. After being left for 3 minutes, 1.2 mL of 7.5% Na_2CO_3 solution was added and left again at room temperature. Absorbance was read with a spectrophotometer at a wavelength of 750 nm. Gallic acid standard solutions were made at concentrations of 15, 20, 25, 30, and 35 µg/mL, each being put into tubes and then added with 1.5 mL of Folin-Ciocalteu reagent (1:10). Afterwards, a calibration curve of the relationship between gallic acid concentration (µg/mL) and absorbance was made (Endah, 2016).

Antihypertensive activity test

The induced test animals in the control group were given a Na-CMC treatment, the Captopril group animals were given a Captopril suspension at a dose of 4.5 mg/kg BW, and the animals in the extract groups were given EEJCL at doses of 1.8, 2.7, and 4.05 g/kg BW, respectively. Treatments were applied orally from day 15 to day 21. Blood pressure measurements were carried out on day 14 for pre-treatment data. Blood pressure measurements were carried out on days 17, 20, and 22. The rats' systolic, diastolic, and mean arterial blood pressures were measured by the non-invasive blood pressure method using the CODA device. A tail cuff was placed on each rat's tail to monitor the rat's blood pressure. This CODA device has a VPR (Volume Pressure Recording) sensor, which uses a differential pressure transducer specifically designed to measure blood volume in the rat's tail non-invasively (Stanisavljevic *et al*., 2022).

LDL test

The induced test animals in the normal and negative groups were given an Na-CMC treatment, the positive group animals were given Simvastatin at 0.9 mg/kg BW, and the animals in the extract groups were given EEJCL at doses of 1.8, 2.7, and 4.05 mg/kg BW, respectively. Blood sampling was carried out twice, before and after treatment, with the rats fasting for ± 12 hours. Blood sampling of 3 mL was carried out through the retro-orbital sinus after the rats were anesthetized with ether (Nurmeilis, 2015). The blood was then centrifuged to obtain the serum. LDL cholesterol level data of the hypertensive Wistar rats given a high-fat diet were then analyzed. The enzymatic colorimetric test method was employed to directly measure LDL cholesterol levels.

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Table 1. TLC results on flavonoid content

Sample	Rf	Detection			Flavonoid
		UV 254	UV 366	Ammonia vapor	
Ethanol extract of *Jatropha curcas* leaves	1) 0.50	Yellow	Yellow	Yellow brownish	+
	2) 0.62	Yellow	Yellow	Yellow brownish	+
	3) 0.68	Yellow	Yellow	Yellow brownish	+
	4) 0.87	Yellow	Yellow	Yellow brownish	+
Quercetin	0.53	Greenish yellow	Greenish yellow	Yellow	+

HDL test

The induced test animals in the control group were given a CMC-Na treatment, the Simvastatin group animals were given a Simvastatin suspension at a dose of 0.9 mg/kg BW, and animals in the extract groups were given EEJCL at doses of 1.8, 2.7, and 4.05 g/kg BW, respectively. Blood sampling was carried out twice, before and after treatment, on day 15 and day 22. The obtained blood was separated between the serum and plasma. The serum was prepared with CHOD-PAP reagent and read on a UV-Vis spectrophotometer at a wavelength of 546 nm. Calculations were made on the obtained data to obtain HDL levels in blood.

Data analysis

Data analysis was conducted using SPSS with preliminary tests including the Kolmogorov-Smirnov test to determine if the data were normally distributed or not and the Levene test to determine if the variance was homogeneous or not. If the obtained data were normally distributed ($p > 0.05$) and homogeneous ($p > 0.05$), then it was followed by the parametric one-way ANOVA at a 95% confidence level. The analysis proceeded with a post-hoc test using Tukey test to show significant differences between treatment groups.

RESULTS AND DISCUSSION

Extraction of *Jatropha curcas* leaves

Extraction of dried powder from *Jatropha curcas* leaves resulted in 84.7 g of thick extract from a total of 1.7 kg of dried powder, with a yield of 4.98%.

Compounds contained in *Jatropha curcas* leaves based on TLC testing

The results of thin layer chromatography (TLC) testing of the extract after being passed under ammonia vapor in visible light indicated the presence of flavonoid compounds, with Rf 0.50. The ethanol extract of jatropha leaves was positive for flavonoids, as can be seen from the chromatogram profile in Figure 1. The TLC identification data of the ethanol extract of jatropha leaves can be seen in Table 1.

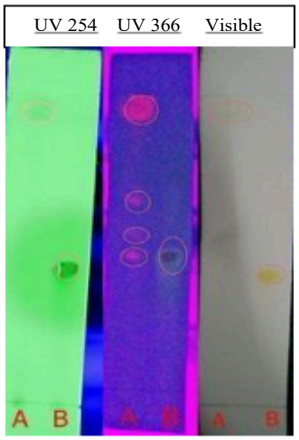

Figure 1. Flavonoid chromatogram profile of the ethanol extract of jatropha leaves: (A) *Jatropha curcas* L. sample; (B) quercetin standard

The results indicated that the ethanol extract of *Jatropha curcas* leaves contained phenolic compounds, with Rf 0.18. The ethanol extract of jatropha leaves was positive for phenolics, as can be seen from the chromatogram profile in Figure 2. The TLC identification data of the ethanol extract of jatropha leaves can be seen in Table 2.

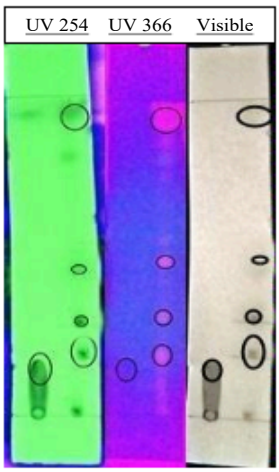

Figure 2. Phenolic chromatogram profile of the ethanol extract of jatropha leaves: (A) *Jatropha curcas* L. sample; (B) gallic acid standard

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Table 2. TLC results on phenolic content

Sample	Rf	Detection			Phenolic
		UV 254	UV 366	$FeCl_3$	
Ethanol extract of *Jatropha curcas* leaves	1) 0.18	blackout	Yellow	Black Grey	+
	2) 0.25	blackout	Yellow	Black Grey	+
	3) 0.43	blackout	Yellow	Black Grey	+
	4) 0.93	blackout	Yellow	Black Grey	+
Quercetin	0.12	blackout	Blue	Black Grey	+

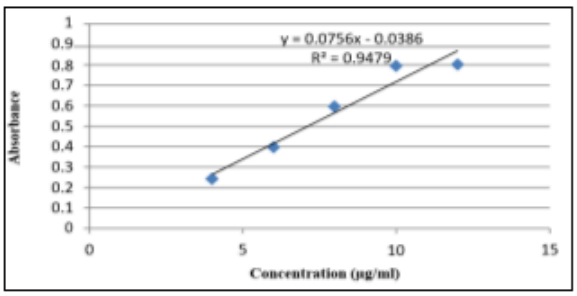

Figure 3. The concentration and absorbance graph of quercetin standard solution

Table 3. Total flavonoid content of the ethanol extract of jatropha leaves

Extract Weight (mg)	Absorbance	Total Flavonoid Content (%)
10.1	0.640	4.43
10.1	0.641	4.44
10.2	0.636	4.36
	Mean ± SD	4.41 ± 0.04

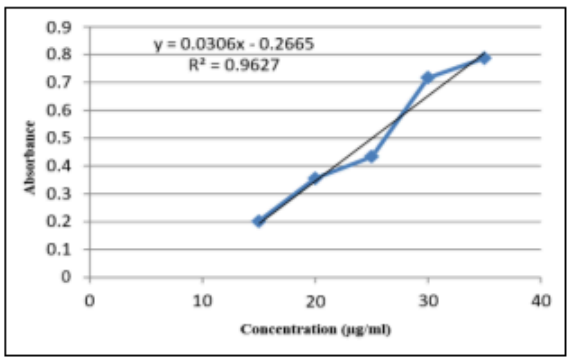

Figure 4. The concentration and absorbance graph of gallic acid standard solution

Table 4. Total phenolic content of the ethanol extract of jatropha leaves

Extract Weight (mg)	Absorbance	Total Phenolic Content (%)
10.1	0.422	11.1
10.3	0.466	11.6
10.5	0.404	10.4
	Mean ± SD	11.03 ± 0.60

Testing of total flavonoid and phenolic contents

Based on testing, the ethanol extract of jatropha leaves had a total flavonoid content of 4.41 ± 0.04%. A quercetin standard curve was developed based on this result, from which a linear regression equation as seen in Figure 3 was produced. The calculation results of flavonoid levels in the ethanol extract of jatropha leaves can be seen in Table 3.

Further testing showed that the ethanol extract of jatropha leaves had a total phenolic content of 11.03 ± 0.60%. A gallic acid standard curve was developed based on this result, from which a linear regression

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E-ISSN: 2580-8303

equation as seen in Figure 4 was produced. Calculation results on phenolic levels in the ethanol extract of jatropha leaves can be seen in Table 4.

The values obtained were above the total phenolic and flavonoid contents previously calculated by Sadik *et al*. (2017), who conducted extraction using the same method and solvent, where the total flavonoid and phenolic contents obtained were 1.48 ± 0.01% and 5.51 ± 0.01%, respectively. The differences in results were possibly due to differences in environmental conditions, such as temperature, soil, and plant cultivation processes.

Antihypertensive testing

The study was conducted on 7 groups of test animals, each consisting of 5 rats. Blood pressure measurements were conducted on days 14, 17, 20, and 22. The results obtained from each measurement can be seen in Tables 5, 6, and 7.

The data of systolic blood pressure measurement (Table 5) indicate that the administration of the ethanol extract of *Jatropha curcas* leaves (EEJCL) was able to lower systolic blood pressure. The most effective EEJCL dose according to these data was 2.7 g/kg BW, which could render a decrease greater than the comparative group (Captopril). A previous study by Sadik *et al.* (2021) also discovered that plants containing flavonoid compounds can lower blood pressure. Flavonoids can inhibit ACE by forming chelate complexes at the active centre of ACE, depending on their main structural features. The flavonoid content in the extract, as well as its antioxidant activity, supports the extract's ability as an antihypertensive agent (Guerrero *et al*., 2012). The one-way ANOVA results on systolic blood pressure showed a significant value ($p < 0.05$), meaning that there was an effect of decreasing systolic blood pressure after the application of the preparation. Therefore, it can be concluded that the ethanol extract of *Jatropha curcas* leaves (EEJCL) is effective as an antihypertensive on male Wistar strain rats.

The diastolic blood pressure measurement data (Table 6) indicate that the administration of the ethanol extract of *Jatropha curcas* leaves (EEJCL) was able to lower diastolic blood pressure. The most effective EEJCL dose according to the data was 2.7 g/kg BW, which could render a decrease greater than the comparative group (Captopril). The one-way ANOVA results on diastolic blood pressure showed a significant value ($p < 0.05$), meaning that there was an effect of decreasing diastolic blood pressure after the application of the preparations. This result supports the conclusion previously drawn.

Table 5. Systolic blood pressure measurement results on days 14, 17, 20, and 22

Group	Dose (g/kg BW)	Mean systolic blood pressure (mm Hg) ± SD			
		D-14	D-17	D-20	D-22
Normal	-	119.0 ± 6.51	123.0 ± 9.13	117.0 ± 5.56	120.0 ± 8.24*
Control	-	151.0 ± 7.74	145.8 ± 2.77	155.8 ± 6.91	137.4 ± 5.40
Captopril	0.0045	148.6 ± 12.4	122.8 ± 3.19*	118.0 ± 5.65*	121.4 ± 9.55*
EEJCL	1.8	143.2 ± 3.96	126.2 ± 10.98	126.4 ± 12.19*	114.8 ± 9.75*
	2.7	143.8 ± 11.88	141.0 ± 13.43	129.8 ± 18.55*	113.4 ± 8.26*
	4.05	139.6 ± 6.18	130.2 ± 17.15*	127.0 ± 16.53*	118.0 ± 8.71*

*)$p < 0.05$, indicating a significant difference from the control group

Table 6. Diastolic blood pressure measurement results on days 14, 17, 20, and 22

Group	Dose (g/kg BW)	Mean diastolic blood pressure (mm Hg) ± SD			
		D-14	D-17	D-20	D-22
Normal	-	84.8 ± 5.89*	76.6 ± 12.01*	76.8 ± 11.73*	73.0 ± 5.52*
Control	-	115.4 ± 7.19	116.2 ± 20.48	114.8 ± 16.33	92.8 ± 6.30
Captopril	0.0045	100.4 ± 26.85	99.0 ± 14.91	90.6 ± 12.30*	91.8 ± 20.50*
EEJCL	1.8	111.8 ± 6.05	99.6 ± 12.15	91.8 ± 15.62*	78.0 ± 7.71*
	2.7	109.0 ± 10.29	102.0 ± 12.58	95.0 ± 16.07*	77.6 ± 12.46*
	4.05	112.2 ± 9.36	94.4 ± 18.82*	90.0 ± 17.91*	81.8 ± 13.14*

*)$p < 0.05$, indicating a significant difference from the control group

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Table 7. Mean arterial blood pressure measurement results on days 14, 17, 20, and 22

Group	Dose (g/kg BW)	Mean arterial blood pressure (mm Hg) ± SD			
		D-14	D-17	D-20	D-22
Normal	-	98 ± 8.97	92.6 ± 7.40	94.4 ± 5.17	88.4 ± 6.02*
Control	-	127.8 ± 6.26	108.4 ± 12.3	128.2 ± 16.55	110.8 ± 14.75
Captopril	0.0045	123.4 ± 10.23	129 ± 19.27*	98.8 ± 8.40*	93.8 ± 6.64*
EEJCL	1.8	119 ± 5.47	115.6 ± 18.35	103.6 ± 15.37*	89.8 ± 7.56*
	2.7	118.6 ± 10.33	113.2 ± 10.35	106.4 ± 16.63*	90 ± 11.37*
	4.05	117.8 ± 10.32	98 ± 19.91*	105.2 ± 13.4*	90.6 ± 9.76*

*) $p < 0.05$, indicating a significant difference from the control group

Table 8. LDL level measurement results (mg/dL) after application of Simvastatin and the ethanol extract of *Jatropha curcas* leaves (EEJCL)

Group	Dose (g/kg BW)	Day-15[1)] (Mean ± SD)	Day-22[2)] (Mean ± SD)	Difference (Mean ± SD)	Decrease percentage (%)
Normal	-	24.25 ± 2.41	22.92 ± 4.64	1.33 ± 3.79*	5
Control	-	36.64 ± 1.58	48.56 ± 3.01	-11.91 ± 4.01	-32
Simvastatin	0.0009	42.74 ± 1.64	24.70 ± 1.89	18.04 ± 2.91*	42
EEJCL	1.8	37.82 ± 4.97	27.57 ± 3.90	10.24 ± 5.25*	27
	2.7	38.53 ± 2.87	26.16 ± 1.94	12.37 ± 4.02*	32
	4.05	38.47 ± 1.97	24.15 ± 1.22	14.31 ± 1.48*	37

*) $p < 0.05$, indicating a significant difference from the control group
1) Day 15, after being given high-fat feed and NaCl at 3.75 g/kg BW for 14 days
2) Day 22, after being given the ethanol extract of *Jatropha curcas* leaves (EEJCL) for 7 days

The mean arterial blood pressure measurement data (Table 7) show that the administration of the ethanol extract of *Jatropha curcas* leaves (EEJCL) was able to lower the mean arterial blood pressure, where the most effective EEJCL dose in this test was 1.8 g/kg BW, with a decrease greater than the comparative group (Captopril). Blood pressure measurements on days 20 and 22 had already shown significant decreases in blood pressure approaching normal. The statistical test results showed a significant difference between the dose groups and the induced groups, while the statistical results of the dose groups compared to the normal and Captopril groups showed no significant difference. The flavonoid compounds in the *Jatropha curcas* leaf ethanol extract exhibited ACE inhibitory activity, which was induced by the formation of chelate complexes at the ACE active centre; this activity depends on the main structural features of flavonoids. The flavonoid content in the extract, and its proven antioxidant activity, supports the extract's ability as an antihypertensive (Dhianawaty *et al*., 2018). As a result, the blood pressure of test rats in the EEJCL 1.8, EEJCL 2.7, and EEJCL 4.05 groups could be lowered approaching normal.

LDL testing

LDL level measurements were also conducted on all the test groups on days 15 and 22, the results of which can be seen in Table 8.

The statistical test results of the EEJCL 1.8, EEJCL 2.7, and EEJCL 4.05 groups showed a significant difference ($p < 0.05$) from the control group. The Simvastatin group was also significantly different ($p < 0.05$) from the control group. The EEJCL 1.8 and EEJCL 4.05 groups showed no significant difference ($p > 0.05$) from the Simvastatin group. Finally, the EEJCL 2.7 group showed a significant difference ($p < 0.05$) from the Simvastatin group. This shows that the administration of EEJCL could lower LDL levels, but not to the extent of normal levels. The data of the difference in rat LDL levels can be seen in Table 8.

The decreases in blood pressure and LDL levels are related to the presence of flavonoid compounds. Various studies have proven that flavonoids can lower blood pressure and LDL levels by inhibiting angiotensin-converting enzyme and binding free radicals and metal ion transitions in inhibiting lipid peroxidation (Loh *et al*., 2020). Flavonoids have the ability to stop oxidative damage and LDL oxidation. In addition, luteolin derivatives can trigger cholesterol barrier secretion, meaning cholesterol levels decrease. When cholesterol is transported from the intestine to the liver, flavonoids function as inhibitors of the HMGCoA reductase enzyme, the enzyme responsible for converting acetyl-CoA to mevalonate in cholesterol synthesis, thus reducing synthesis (Nuralifah *et al*., 2020). Thus, the administration of the ethanol extract of *Jatropha curcas* leaves (EEJCL) for 7 days can lower LDL levels in hypertensive rats given a high-fat diet.

P-ISSN: 2406-9388
E-ISSN: 2580-8303

Table 9. HDL level measurement results (mg/dL) after application of Simvastatin and the ethanol extract of *Jatropha curcas* Leaves (EEJCL)

Groups	Dose (g/kg Bw)	Day15[1)] (Mean ± SD)	Day-22[2)] (Mean ± SD)	Difference (Mean ± SD)	Decrease percentage (%)
Normal	-	34.57 ± 1.17	36.67 ± 0.78	2.09 ± 1.63*	5
Control	-	23.39 ± 1.89	26.40 ± 2.38	3.01 ± 2.23	11
Simvastatin	0.0009	24.61 ± 1.21	33.82 ± 0.57	9.18 ± 1.12*	27
EEJCL	1.8	24.58 ± 2.35	27.45 ± 1.49	2.87 ± 1.56*	10
	2.7	24.58 ± 3.29	29.64 ± 1.49	5.05 ± 2.95*	17
	4.05	23.46 ± 2.86	35.60 ± 0.67	12.14 ± 2.32*	34

*)$p < 0.05$, indicating a significant difference from the control group
1) Day 15, after being given high-fat feed and NaCl at 3.75 g/kg BW for 14 days
2) Day 22, after being given the ethanol extract of *Jatropha curacas* leaves (EEJCL) for 7 days

HDL testing

At last, HDL level measurements were conducted on the test groups. The results of these HDL level measurements on day 15 and day 22 in each group can be seen in Table 9.

Before treatment, the control, Simvastatin, EEJCL 1.8, EEJCL 2.7, and EEJCL 4.05 groups had lower HDL levels compared to the normal group (Table 9). This was because groups other than the normal group were given a high-fat diet containing a lot of cholesterol. HDL is said to be low if the level is < 30 mg/dL (Hernáez *et al*., 2019). Then, the HDL levels in each group showed an increase after EEJCL administration. Table 4 shows that there was an increase in HDL levels after the application of the EEJCL treatment in each group. This shows that *Jatropha curcas* leaf ethanol extract is able to increase HDL levels. Previous research by Anigbogu *et al*. (2015) also discovered that *Jatropha curcas* leaf ethanol extract can increase HDL levels. The increase in HDL levels occurred following the administration of the ethanol extract of *Jatropha curcas* leaves, which is known to contain flavonoid compounds.

In this study, the highest HDL level increase occurred in the EEJCL 4.05 group. The effects resulted should go hand in hand with increasing doses. However, higher doses will have decreased effects. This is because the dose can no longer maximally provide effects. This case often occurs in traditional or herbal medicines, in which case these medicine no longer contain a single chemical compound, but several types of chemical compounds that work together to provide effects. It is not impossible that with increasing doses the amount of contained compounds also increases and unwanted reactions that can reduce effects occur (Siskayanti *et al*., 2017).

A similar study was conducted by Abdulmumin (2020), who reported that extracts of *Jatropha Curcas* leaves, peel, stems, and roots have hypolipidemic activity and may be useful in managing cardiovascular diseases. The acute toxicity (LD50) of *Jatropha curcas* leaf, peel, stem, and root extracts was found to be greater than 5,000 mg/kg, thus declared practically non-toxic to experimental animals (Mika'il *et al*., 2020). Administering treatments such as flavonoid-containing EEJCL is likely to increase endothelial nitric oxide (eNOS) synthesis, thus increasing NO bioavailability. Flavonoids can act as vasodilators with suitable signaling pathways and structural characteristics for strong vasorelaxant properties (Loh *et al*., 2020). In other words, the ethanol extract of *Jatropha curcas* leaves has a potential for development in the treatment of hypertension and dyslipidaemia. This study can be a reference for further research on similar topics, with the potential to lead to the development of more promising antihypertensive alternatives.

CONCLUSION

The ethanol extract of *Jatropha curcas* L. (EEJCL) leaves contains flavonoid and phenolic compounds. The administration of EEJCL can reduce blood pressure significantly in terms of systolic, diastolic, and average arterial blood pressure. In addition, it can increase HDL levels and reduce LDL levels in the blood of hypertensive rats given a high-fat diet. Therefore, it is concluded that the ethanol extract of *Jatropha curcas* L. (EEJCL) leaves has a potential for development in the treatment of hypertension and dyslipidaemia.

ACKNOWLEDGMENT

We acknowledge the Dean of the Faculty of Pharmacy and the staff of the Pharmacology Laboratory of Ahmad Dahlan University for supporting the completion of this research.

AUTHOR CONTRIBUTIONS

Conceptualization, M.S.B., W.Y.A., P.D.L., D.E.W., D.R.N., S.Y., W.W., L.H.N.; Methodology, M.S.B., S.Y., L.H.N., D.E., V.S.; Software, M.S.B.,

P-ISSN: 2406-9388
E-ISSN: 2580-8303

L.H.N., M.M.; Validation, M.S.B., S.Y., W.W., L.H.N., D.E., V.S.; Formal Analysis, M.S.B., L.H.N., M.M.; Investigation, M.S.B., S.Y., W.W., L.H.N., D.E., V.S.; Resources, M.S.B., S.Y., W.W., L.H.N., D.E., V.S.; Data Curation, M.S.B., W.Y.A., P.D.L., D.E.W., D.R.N.; Writing - Original Draft, M.S.B., W.Y.A., P.D.L., D.E.W., D.R.N., M.M.; Writing - Review & Editing, M.S.B., S.Y., W.W., L.H.N., D.E., V.S.; Visualization, M.S.B., S.Y., W.W., L.H.N., D.E., V.S.; Supervision, M.S.B.; Project Administration, M.S.B.; Funding Acquisition, M.S.B.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

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P-ISSN: 2406-9388
E-ISSN: 2580-8303