ISSN 2548-6462 (online), ISSN 2088-8740 (print)

DOI: 10.30644/rik.v13i1.836

Test of the effectiveness of the ethyl acetate fraction of dayak onion bulbs (eleutherine bulbosa (mill.) urb) as an antihypertensive

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Accepted: 16 March 2024; revision: 26 June 2024; published: 30 June 2024

Abstract

Background: When blood pressure is higher than normal—that is, when the systolic and diastolic pressures are greater than 140 and 90 mmHg, respectively—it is referred to as hypertension. Dayak onion bulbs are one plant that can reduce blood pressure. This study sought to ascertain if the ethyl acetate component of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) might effectively lower blood pressure in male white rats that were hypertensive.

Method: The study employed an experimental design with 36 male white rats split into 6 groups: dosage group (50, 100, 200 mg/kgbb), comparator group (catopril), negative control, and positive control. For 14 days, an 8% NaCl inducer was applied. A Non-Invasive Blood Pressure (NIBP) gadget is used to measure blood pressure. One Way Anova was utilized in the data analysis, and then the Duncan test was performed.

Results: The injection of Dayak onion bulb ethyl acetate fraction was found to have a substantial (p<0.05) reduction in systolic, diastolic, mean arterial blood pressure, and heart rate.

Conclusion: The analysis concludes that administering the ethyl acetate component at a dose of 200 mg/kgbb is the most effective way to lower blood pressure. The thickness of the left ventricle in mice showed a histological improvement.

Keywords: Antihypertensive; Dayak Onion Bulbs; Histopatholog

INTRODUCTION

An increase in systolic blood pressure of more than 140 mmHg or diastolic blood pressure of more than 90 mmHg is referred to as hypertension (1). According to WHO, the prevalence of hypertension in adults aged 30-79 years varies in various regions, namely the Eastern Mediterranean reaching 37.8%, Europe 36.9%, Africa at 35.5% and America at 35.4%, while the Western Pacific region has the lowest rate was 28.3%. There are gender differences in prevalence. In the Eastern Mediterranean Southeast Asian regions, the prevalence in women is higher than in men. In contrast, in the Americas, Europe and the West Pacific, the prevalence in men is higher than in women (2). Indonesia has a prevalence of hypertension in people over 18 years of age. namely 36.9% for women and 31.3% for men

(3). The prevalence of hypertension in West Sumatra reached 25.16%. Based on measurement results, the number of sufferers in the population aged ≥18 years was more female, reaching 27.69%, while among men it was around 22.51%. The hypertension data results in Bukittinggi reached 31.05%. Bukitinggi is one of the districts/cities with the highest number of hypertension sufferers in West Sumatra (4).

Hypertension is often called the silent killer because it often goes without complaints so sufferers do not know that they have hypertension before having their blood pressure checked. Etiologically, hypertension is divided into two, namely primary hypertension and secondary hypertension. Unknown factors that can cause primary hypertension are humoral abnormalities, disorders of the central nervous system,

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abnormalities in the kidneys, decreased synthesis of compounds that act vasodilators and high sodium uptake (5). secondary hypertension Meanwhile, is caused by other disease factors such as chronic kidney disease, parathyroid disease, renovascular disease and aldosterone. Almost everyone will experience high blood pressure as they get older. Increasing age is problematic factors of the hypertension, especially coronary disease. More than half of deaths over the age of 60 are caused by heart disease(6). Other comorbidities such as hypercholesterolemia or often referred to as high levels of cholesterol in the blood. If a person has high cholesterol levels, it can cause fat to accumulate in the blood vessels, which can affect blood flow to the heart and throughout the body (7).

The use of traditional medicine in Indonesian society is currently growing. Many people are interested in using traditional medicine to treat all the illnesses they suffer from various kinds of Indonesian medicinal plants. Eleutherine bulbosa (Mill) Urb, often known as the Dayak onion plant, is one among them and is said to have multiple therapeutic uses for treating a variety of ailments.Dayak onion bulbs have been shown empirically to treat a variety of conditions, including hypertension, diabetes mellitus, stroke, colon cancer, breast cancer, fever, dysuria, colitis, dysentery, jaundice, boils, cysts, and prostate problems. They can also be used to improve breast milk and treat related to it. (8) Alkaloids, illnesses flavonoids, saponins, terpenoids, steroids, glycosides, tannins, phenolics, anthraquinones are all present in Dayak onion bulbs. Alkaloids, flavonoids, glycosides, anthraguinones, tannins, and triterpenoids/steroids are all present in Dayak onion bulb ethanol extract. Dayak onion bulbs' ethyl acetate fraction has flavonoids, tannins, and phenolic substances (9). Compound Saponins have diuretic properties which can reduce plasma volume by removing water and electrolytes, especially so that cardiac output decreases. Sodium and water can also affect peripheral resistance.

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Flavonoids are efficacious as diuretics, one of which is by removing a number of fluids and electrolytes as well as toxic substances. By reducing the amount of water and salt in the body, the blood vessels will become loose so that blood pressure slowly decreases(9). Based on research (10) Dayak onion extract has antihypertensive activity which can reduce diastolic blood pressure, systolic blood pressure and mean arterial pressure. The secondary metabolite content found in Dayak onions is flavonoids, alkaloids, triterpenoids and steroids.A decrease in diastolic blood pressure and systolic blood pressure occurs becauseThe ena in Dayak onions contains the compound eleutherinol which is an estrogen agonist (11).

Based on the background above, there are many cases of hypertension and the potential of Dayak onion bulbs as antihypertensives. Therefore, researchers want to conduct research on testing the effectiveness of the ethyl acetate fraction of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) as an antihypertensive in male white rats.

RESEARCH METHODS Tool

The tools used in this research were animal cages (rats) along with rat food and drink, test tube racks, test tubes (Tirex), measuring cups (Iwaki), Erlenmeyer (Tirex), measuring pipettes (Tirex), spatula, syringe, spatula, dropper pipette (One Med), mortar and stamper (Iwaki), analytical balance (OHAUS), rotary evaporator (IKA), evaporator cup (Iwaki), animal scale, funnel (Iwaki), oven (Memmert), crucible (Iwaki), furnace (SH Scientific), desiccator (Normax), beaker glass, watch glass, Non-Invasive Blood Pressure (NIBP)-CODA blood pressure measuring device, filter paper, measuring flask, maceration bottle, and stir bar. Material

The materials used are Wistar male white rats, Dayak onion bulbs, captopril, 96% ethanol, distilled water, concentrated hydrochloric acid/HCL, iron chloride (III)/FeCl3, sodium chloride/NaCl, metal/Mg, magnesium sodium carboxymethylcellulose/Na -CMC, ethyl

acetate, Mayer's reagent, Bouchardat's reagent, Dragendorf's reagent.

Method

1. Sample preparation

The samples used in this research were Dayak onion bulbs (Eleutherine Bulbosa (Mill) Urb) taken from Simpang Tiga, Padang Gelugur District, Pasaman Regency, West Sumatra.

2. Sample identification

Samples were identified in the Andalas University Herbarium, Biology Department, FMIPA, Andalas University.

3. Extraction

Dayak onion bulb extract (Eleutherine bulbose (Mill.) Urb.) is made by maceration. 200 grams of Dayak onion powder were weighed, then placed each in a dark (brown) glass bottle intended to protect from sunlight. The bottle filled with Dayak onion simplicia powder was filled with 1000 ml of 96% ethanol solvent, then left for 3 days in a room that was not exposed to direct sunlight and was shaken occasionally. The resulting macerate is filtered with flannel cloth to separate the filtrate from the dregs. The filtrate obtained was concentrated using a rotary evaporator until it was concentrated. Store the extract in a well-closed place (13).

4. Evaluation of extracts Organoleptic

This organoleptic examination is carried out to see the physical appearance of the extract by visual observation which includes color, shape, smell and taste (13).

Rendement

Yield is a comparison between the extract obtained and the initial simplicia (13).

Drying shrinkage

Add approximately 1 gram of extract and weigh carefully in a balanced container. Dry at 105 °C for 5 hours and weigh. Continue drying and weighing 1 hour apart until the difference between 2 consecutive weighings is no more than 0.25%.

Phytochemical test

Flavonoid test

The sample was taken with a spatula, followed by four drops of 2% HCl and four spatulafuls of magnesium powder added.

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The filtrate will turn orange-red in hue, signifying the presence of flavonoids.

Tannin test

One or two drops of 1% iron (III) chloride reagent were added to the extract in a test tube. A shift in the filtrate's hue to green or blackish blue will indicate the presence of tannins.

Alkaloid test

After adding a few drops of 2 N HCl and distilled water to the extract to be analyzed, it is heated over a water bath for two minutes, cooled, and filtered. The following filtrate was utilized in the alkaloid test:

Following the addition of two drops of Mayer's reagent solution and three drops of filtrate, observations were made.

Following the addition of two drops of Bouchardat's reagent solution and three drops of filtrate, observations were made. Following the addition of two drops of the dragendrof reagent solution and three drops of filtrate, observations were made. If silt or turbidity appears in two or more of the aforementioned three trials, alkaloids are positive. The production of a brownish yellow hue with Dragendorf's reagent and a yellow precipitate with Meyer's reagent are indicative of a positive alkaloid reaction.

Test for steroids and triterpenoids

The extract to be examined is put into a test tube, then 2-3 drops of anhydrous acetic acid are added, then stirred slowly for a few moments until dry, then 1-2 drops of concentrated sulfuric acid are added and the coloring that appears is observed. Red or red-violet staining gives an indication of triterpenoids while green-blue staining is for steroids.

1. Fractionation

The thick extract was fractionated liquidliquid with a ratio of 1:1. First, use 50 ml of water and 50 ml of n-hexane 3 times using a separating funnel until 2 clearly separated layers of liquid are formed. The n-hexane fraction was separated from the water fraction then collected in a different container and then concentrated using a

rotary evaporator at a temperature of 40°C. Second, the water fraction was then in the liquid-liquid fraction again with 50 ml of ethyl acetate 3 times using a separating funnel to form 2 real layers. The ethyl acetate fraction and water fraction were separated in different containers and then concentrated using a rotary evaporator (12).

2. Preparation of 0.5% Na CMC solution (7)

Sprinkle 500 mg of Na CMC in 10 ml of hot water that has been put into a hot mortar, let it sit for 15 minutes, then grind until homogeneous and dilute with distilled water to a volume of 100 ml.

3. Preparation of 8% NaCl induction solution (7)

Weighed 8 grams of NaCl, dissolved it in distilled water to a volume of 100 ml.

4. Making a comparison drug (captopril)

A total of 25 mg of captopril was put into a measuring flask, then 10 ml of distilled water was added, so that a captopril concentration of 25 mg/10 ml or 2500 ppm was obtained.

5. Preparation of fraction preparations

The thick fraction of Dayak onion bulbs was weighed respectively as 0.05 g (dose 50 mg/kgBW), 0.1 g (dose 100 mg/kgBW) and 0.2 g (dose 200 mg/kgBW). Then each dose was suspended in 0.5% Na CMC up to 100 ml.

6. Grouping Test Animals

Three months old, 36 male Wistar white rats weighing between 160 and 180 g were the experimental animals.

Before being given treatment, the mice were acclimatized for one week to adapt to their environment. Food and drink during maintenance are given in moderation, the animals are weighed, and their behavior is The mice used observed. for the experiment were mice that were healthy, is, considered that during maintenance the mice's body weight did not decrease by more than 5% and visually showed normal behavior. (14).

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Table 1.Grouping Test Animals

Group	Giving						
1	Negative Control (eating and						
	drinking)						
2	Positive Control (NaCl)						
3	Ethyl Acetate Fraction of Dayak						
	Onion Bulbs 50 mg/kgbb						
4	Ethyl Acetate Fraction of Dayak						
	Onion Bulbs 100 mg/kgbb						
5	Ethyl Acetate Fraction of Dayak						
	Onion Bulbs 200 mg/kgbb						
6	Comparative Group (captopril)						

Each group received the preparation orally once daily, as indicated in the above table, and their blood pressure was measured using the Non-Invasive Blood Pressure (NIBP) method. Four factors are used to assess blood pressure: heart rate, mean arterial blood pressure, diastolic blood pressure, and systolic blood pressure. Blood pressure measurements were carried out three times, namely blood pressure (normal), blood pressure after NaCl induction for 14 days and blood pressure after administration of Dayak onion bulb ethyl acetate fraction for 7 days.

7. Histopathology Test

The heart organ was made into a histology preparation with a thickness of 5µm and stained with hematoxylin and eosin (H&E). Observed in the myocardial layer of the left ventricle (15).

Data analysis

Data analysis used one-way ANOVA statistics and continued with the Duncan test.

RESULTS AND DISCUSSION

When arterial blood pressure rises, it is referred to as hypertension. Systolic blood pressure must be greater than 140 mmHg, and diastolic blood pressure must be greater than 90 mmHg. (16). According to (17) the compounds contained in Dayak onions are naphthalene, napthoquinone, and anthraquinone. Compounds that act as antihypertensives are eloutherol, isoeluterine, and eleutherine. This compound is able to widen blood vessels so that strong systolic pressure can be overcome (18).



Figure 1. Dayak Onion Bulbs

Based on the plant identification results, it shows that the Dayak onion bulb samples belong to the species (Eleutherine bulbosa (Mill) Urb) from the Iridaceae family. The yield of Dayak onion bulb extract was 7.47% and the drying loss was 1.9550%. The standard yield value according to the herbal supplement pharmacopoeia is not less than 26% (13), the

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yield value does not meet the requirements. (13) states that the drying shrinkage test requirement is <10%, so that the drying shrinkage value meets the requirements. Drying loss is a parameter of the presence of substances other than water which aims to provide a maximum limit (range) of the amount of compounds lost in the drying process (13). The organoleptic test results of the extract showed a reddish-brown color, thick extract and a distinctive odor.

The results of phytochemical screening of fractions demonstrated extracts and outcomes for the secondary favorable metabolite chemicals terpenoids, alkaloids, flavonoids, and tannins. According (10) research, the Dayak onion bulb extract's (Eleutherine bulbosa (Mill) Urb) phytochemical screening results contained alkaloids, triterpenoids flavonoids, steroids which were one of the secondary metabolite compounds used for antihypertensive testing in this study.

Table 2. Phytochemical Screening Results

No	Chemical content	Reactor	Parameter	Extract	Fraction
1	Flavonoids	Mg + HCL	Orange, brick red, pink and dark red colors are formed	+	+
2	Phenol	Fecl3	Blackish green-blue in color	-	-
3	Tannin	Fecl3	Dark brown or blackish blue in color	+	+
4	Alkaloids	HCL 2N + meyer's reager dragendrof's reagent and Bouchardat		+	+
5	Steroids	Liberman Boucart reagent	's Blue or purple in color	-	-
6	Terpenoids	Liberman Boucart reagent	's Red in color	+	+

Description: (+): reacts to color change (-): does not react

Induction of 8% NaCl was given for 14 days with the aim of increasing the blood pressure of the rats until they reached hypertensive conditions so that the therapeutic effect could be seen which would be tested on male white rats. NaCl 8% is a preparation that has a high salt

intake which can increase the volume of extracellular fluid in the body thereby increasing cardiac output and causing an increase in blood pressure (19).

Normal blood pressure (normotension)in male white mice, the systolic blood pressure is 129 mmHg, diastolic 90 mmHg, and heart

rate 350-450 mmHg (20). Rats that exceed normal blood pressure can be interpreted as having hypertension, which will then be followed by administration of Dayak onion bulb ethyl acetate fraction preparations. According to (11), that Dayak onion

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bulbscontains the compound eleutherinol which has been reported to bind to estrogen receptors in silico studies. Blood lipid profiles are assumed to have decreased, avoiding atherosclerosis and lowering blood pressure in hypoestrogen-treated rats.

Blood Pressure Measurement Results

1. Systolic Blood Pressure

		Post	Decrease	%	Mean and SD
Group	Pre (mmHg)	(mmHg)	(mmHg)	Decline	
Negative Group	145.67	124	21.67	15%↓	21.67 ± 5.77 a*b
Positive Group	150.33	162.33	-12.00	-8%↑	-12 ± 14.17 a
FBD group 50					57.67 ± 19.08 b*c
mg/kgbb	153	94.83	58.17	38%↓	
FBD group 100					70.67 ± 11.37 c
mg/kgbb	180.67	109.77	70.90	39%↓	
FBD group 200					33.67 ± 20.79 b*c
mg/kgbb	151.33	117.23	34.10	23%↓	
Comparative					33.67 ± 44.24 b*c
Group (catopril)	127.93	94.07	33.86	26%↓	

Table 3.Systolic Blood Pressure Measurement Results **Information**: a,b,c same superscript with different columns

Based on the picture above, there was a decrease in the average blood pressure in each test group after being given treatment, except for the positive control group, because the positive control group was given 8% NaCl induction until the end without treatment. The results showed that administration of the Dayak onion bulb ethyl acetate fraction (Eleutherine bulbosa(Mill) Urb) has a significant effect with captopril in reducing blood pressure which is the greatest compared to other doses. The comparison group (captopril) experienced a decrease in blood pressure because captopril is the first line therapy in the treatment of hypertension which is included in the ACE group which works to prevent the change of angiotensin I to angiotensin II, resulting in vasodilation. The negative control group experienced a decrease that was not very significant because this group was not given any treatment from start to finish. Meanwhile, the test experienced a significant decrease in average systolic blood pressure because they were treated with ethyl acetate and captopril fractions which were useful in lowering blood pressure. The researcher's assumption is that the ethyl acetate fraction of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) can reduce systolic blood pressure.

This is confirmed by research conducted by (19) regarding the test of the effect of Dayak onion (Eleutherine americana Merr.) ethanol extract as antihypertensive on male white rats (Rattus norvegicus) showed a decrease in systolic blood pressure of ≥ 20 mmHg at a dose of 200 mg/kgbb, dose of 400 mg/kgbb and a dose of 600 mg/kgbb. The antihypertensive activity shown by Dayak onions works in various ways, namely reducing peripheral resistance of blood vessels and affecting the work of the heart itself. Thompson states that if a test material can lower systolic blood pressure by at least 20 mmHg, it is considered to have an antihypertensive effect (21). After delivering the test preparation, there was an effect of lowering systolic blood pressure, as indicated by the significant difference (0.020<0.05) in the one-way ANOVA statistical test findings. The dose of 200 mg/kgbb is the most efficient in lowering systolic blood pressure, according to the Duncan test, which also

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yields significant results when compared to the comparison group (captopril). The ethyl acetate fraction of Dayak onion bulbs (Eleutherine Bulbosa (Mill) Urb) has been found to be useful in treating male white rats with hypertension. According to other studies, another natural plant, known as mahogany seed ethanol extract, can also lower systolic blood pressure. The most effective dose to reduce systol blood pressure is 200 mg/kgbb (22).

2. Diastolic Blood Pressure

Table 4. Diastolic Blood Pressure Measurement Results

		Post	Decrease	%	Mean and SD
Group	Pre (mmHg)	(mmHg)	(mmHg)	Decline	
N 0	440.00	22.22	47.07	450/	17.67 ± 17.21 b*c
Negative Group	116.00	98.33	17.67	15%↓	
					-10.33 ± 12.34 a
Positive Group	126	136.33	-10.33	-8%↑	
Ethyl Acetate Fraction					35.22 ± 11.59 c
Group 50 mg/kg BW	110.33	74.77	35.56	32%↓	
Ethyl Acetate Fraction					68 ± 17.52
Group 100 mg/kg BW	151.33	96.17	55.16	36%↓	d
Ethyl Acetate Fraction	•				9.33 ± 7.57
Group 200 mg/kg BW	113	103.43	9.57	8%↓	a*b
Comparative Group					3.33 ± 4.50
(captopril)	87.93	85.4	2.53	3%↓	a*b

Information: a,b,c same superscript with different columns

The results of reducing blood pressure can be seen in the table above where the administration of the ethyl acetate fraction of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) has a significant effect with the administration of the drug captopril in reducing blood pressure. The negative control group experienced a decrease that was not very significant because this group was not given any treatment from start to Meanwhile, finish. the test experienced a significant decrease in the average diastolic blood pressure because they were treated with ethyl acetate and captopril fractions which were useful in lowering blood pressure. The ethyl acetate portion of Dayak onion bulbs, or Eleutherine bulbosa (Mill) Urb, is thought by the researcher to have the ability to lower diastolic blood pressure. Research (10),

which shown that administering Dayak onion extract at a dose of 100 mg/kgbb had an impact on lowering blood pressure, supports this. The presence of eleutherine, isoeleutherine. eleutherol shows increase in coronary flow in the guinea pig liver (23). The results of one-way ANOVA statistical testing followed by the Duncan test showed significant results between the comparison group (captopril) and the 200 mg/kgbb dose group. Another study (Natural ingredients) also states that matoa leaf extract and fraction are able to reduce hypertension and cholesterol levels in the blood, the most effective dose of 300 mg/kgbb (21).

3. Mean Arterial Pressure

Table 5. Average Arterial Measurement Results

	Pre	Post	Decrease		Mean and SD
Group	(mmHg)	(mmHg)	(mmHg)	% Decrease	
					19.33 ± 13.42
Negative Group	125.67	106.33	19.34	15%↓	b
Positive Group	133.67	149	-15.33	-11%↑	-15.33 ± 5.50 a

Ethyl Acetate					42.67 ± 10.69 c
Fraction Group					
50 mg/kg BW	124.33	81.23	43.1	35%↓	
Ethyl Acetate					
Fraction Group					69 ± 15
100 mg/kg BW	169.67	100.37	69.3	41%↓	d
Ethyl Acetate					17.67 ± 9.07 b
Fraction Group					
200 mg/kg BW	125.67	107.77	17.9	14%↓	
Comparative					15 ± 14.52 b
Group (captopril)	103.5	88	15.5	15%↓	

Information: a,b,c,d same superscript with different columns

The results of reducing average arterial pressure can be seen in the table above that the administration of Dayak onion bulb ethyl acetate fraction (Eleutherine bulbosa (Mill) Urb) provides a significant effect with administration of the drug captopril. The negative control group experienced a decrease that was not very significant because this group was not given any treatment from start to finish. Meanwhile, the test group experienced a significant decrease in mean arterial pressure because they were treated with ethyl acetate and captopril fractions which were useful in

lowering blood pressure. The ethyl acetate component of Dayak onion Eleutherine bulbosa (Mill) Urb, is thought by the researcher to have the ability to lower average arterial pressure. The study conducted (10) confirms that a dose of 100 mg/kgbb of Dayak onion tuber extract (Eleutherine Americana) can lower average pressure. One-way arterial ANOVA statistical testing and the Duncan test revealed significant differences between the 200 mg/kgbb dosage group and the comparison group (captopril).

4. Heart rate

Table 6. Heart Rate Measurement Results

	Pre	Posts	Decrease	%	Mean and SD
Group	(times/minute)	(times/minute)	(times/minute)	Decline	
Negative Croup	404.00	225 22	00	220/	99 ± 58.94 b
Negative Group	424.33	325.33	99	23%↓	
Positive Group	351	428.33	-77.33	-22%↑	-77.33 ± 106.35 a
Ethyl Acetate					
Fraction Group 50					
mg/kg BW	421	204	217	52%↓	217 ± 102.80 b
Ethyl Acetate					
Fraction Group 100					
mg/kg BW	333	266.33	66.67	20%↓	66.67 ± 77.02 a*b
Ethyl Acetate					
Fraction Group 200					
mg/kg BW	423	206.03	216.97	51%↓	216.67 ± 55.30 b
Comparative Group				·	·
(captopril)	288.33	154.13	134.2	47%↓	130.67 ± 122.31 b

Information: a,b same superscript with different columns

The results of the decrease and increase in heart rate can be seen in the table above that the administration of the ethyl acetate fraction of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) provides a significant effect with the

administration of the drug captopril. The negative control group experienced a decrease that was not very significant because this group was not given any treatment from start to finish. Meanwhile, the

test group experienced a significant decrease in heart rate because they were treated with ethyl acetate and captopril fractions which were useful in lowering blood pressure. The researcher's assumption is that the ethyl acetate fraction of Eleutherine bulbosa (Mill) Urb, the Dayak onion bulb can reduce heart rate. The results of one-way ANOVA statistical testing followed by the Duncan test showed significant results between the comparison group and the 200 mg/kgbb dose group. This is confirmed by research conducted (10) explained that administering Dayak onion extract at a dose of 400 mg/kgbb showed significant results in reducing heart rate.

5. Histopathology Test of Heart Organs in Rats

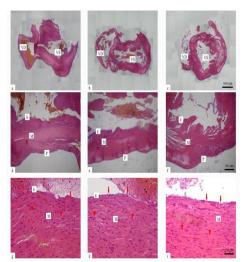


Figure 2. Rat Heart Histopathology

Description: left ventricle (VS), and right ventricle (VD). Endocardium (E), myocardium (M), pericardium (P), endothelial cells (arrow ↓) and cardiac muscle cells (arrowhead ▼). Hypertension control group (NaCL) (a, d, g), treatment with the comparison drug captopril (b, e, h), treatment with 100mg Dayak onion (c, f, i,).

Histological assessment of the effect of the ethyl acetate fraction of Eleutherine bulbosa (Mill) Urb, the Dayak onion bulb as an antihypertensive in male white rats showed differences between the control and treatment groups. In the positive control group (hypertension) there was no visible heart with thick left ventricular muscle. This can be caused by the effects

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of left ventricular muscle hypertrophy, which is often found in hypertension, as an adaptive response of the heart muscle due to increased peripheral blood pressure. In this study there was a negative control group (normal animals without hypertension), so that the normal value of the base thickness of the left ventricular muscle of normal animals could be determined. Animals given the standard drug captopril showed lower left ventricular muscle layer thickness than hypertensive controls.

This shows the effect of controlling peripheral blood pressure, so that left ventricular hypertrophy can be reduced. Administration of Dayak onion bulb fraction (Eleutherine bulbosa (Mill) Urb) showed that the thickness of the left ventricular muscle myocardium layer was lower than that of hypertension controls but still higher than standard drug treatment.

This gives the impression that there is prevention of cardiac hypertrophy due to hypertension when giving Dayak onion bulbs, this illustrates the positive effect of using Dayak onion bulbs on the heart of hypertensive animals. However, the effect of preventing hypertrophy is still below standard drugs.

In the experimental animal group, the endothelial and heart muscle cells appeared to be within normal limits, there were no signs of necrosis of the endothelial cells or heart muscle cells. In the initial phase of hypertension treatment, there is usually no damage to the heart muscle, in the later phase muscle hypertrophy can be found but without death of muscle or endothelial cells. Damage to muscle and endothelial cells in the new heart is found in the advanced phase and long-standing hypertension. In this study, hypertension carried out did not show severe or chronic hypertension, so there were no signs of heart muscle cell death. Administration of either captopril or Dayak onion bulbs also did not show damage to heart muscle cells. This provides data that a dose of Dayak onion bulbs can improve the thickness of the post-hypertension

heart while also showing no toxic effects on the endothelium and heart muscle cells.

CONCLUSION

It is possible to draw the following conclusions from the research on the efficacy of the ethyl acetate fraction of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) as an antihypertensive agent in male white rats: Blood pressure can be lowered by the ethyl acetate fraction of Dayak onion bulbs. At an effective dose of 200 mg/kgbb, the ethyl acetate component of Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb) reduces systolic, diastolic, and average arterial blood pressure as well as heart rate. Administration of the ethyl acetate fraction Dayak onion bulbs (Eleutherine bulbosa (Mill) Urb at doses (50 mg/kgbb, 100 mg/kgbb, 200mg/kgbb) have the same effect as the comparison drug (captopril) in lowering blood pressure. There is a histopathological improvement in left ventricular muscle thickness hearts experimental animals with hypertension after administration of Dayak onion bulb ethyl acetate fraction (Eleutherine bulbosa (Mill) Urb). There were no signs of cell damage, either degeneration or cell necrosis in all treatment groups of experimental animals with hypertension.

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