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Benefits of Inggir-Inggir Fruit (Solanum Sanitwongsei Craib.) for Reducing Hypertension Pressure

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ABSTRACT

Hypertension is one of the silent killer diseases known as cardiovascular disease. Increased blood pressure and an unbalanced lifestyle can increase the risk factors for the emergence of various diseases such as coronary arteries, heart failure, stroke, and kidney failure. The purpose of this research is to determine the blood pressure lowering effect of inggir-inggir fruit ethanol extract on normotensive Wistar rats and to determine the blood pressure lowering effect of inggir-inggir fruit ethanol extract on hypertensive Wistar rats. This study uses an experimental method that is to determine the effect of the independent variable on the dependent variable with the research stages. The results of statistical analysis showed that the EEBI group doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw were not significantly different (p> 0.05) with the control group (CMC-Na 0.5%) or the positive comparison group (bisoprolol) in reducing TDS, TDD, DJ and TAR of normotensive Wistar rats. The results of statistical analysis showed that EEBI doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw can reduce TDS, TDD, and TAR of hypertensive Wistar rats significantly (p < 0.05) compared to the normal group without any administration and the CMC-Na 0.5% control group but could not reduce the DJ of hypertensive Wistar rats significantly (p> 0.05) with the normal group without any administration and the CMC-Na 0.5% group. EEBI dose of 50 mg/kg bw is the best group to reduce TDS, TDD and TAR.

Keywords: *Ethanol extract, wistar, rats, hypertension*

1. INTRODUCTION

Hypertension is one of the silent killers known as cardiovascular disease. Increased blood pressure and an unbalanced lifestyle can increase the risk factors for diseases such as coronary artery disease, heart failure, stroke and kidney failure. One study stated that patients who discontinued antihypertensive therapy were five times more likely to have a stroke. This disease is one of the contributors to high medical costs due to the high number of visits to the doctor, hospitalization and/or long-term drug use.

According to Ikeda, et al. (2014), the largest contributor to hypertension in the world is America with a prevalence of 83.9% in 2009-2010 occurring at the age of 35-49 years. (Ikeda, N., Sapienza, D., Guerrero, R., Aekplakorn, W., Naghavi, M., Mokdad, H.A., Lozano, R., Murray, C., dan Lim, 2014). In Indonesia, the prevalence of hypertension is 25.8% at the age of ≥18 years. Most hypertensive patients come from the lower middle class who live in urban areas with unemployment status (Hastoety et al., 2018). The high cost of chemical drugs to treat hypertension cannot be borne by the economically weak so that herbal medicines become the main alternative.

Many traditional treatments have been recommended as alternatives to treat hypertension. The mechanism of herbal medicine in the treatment of hypertension is not yet known with certainty. Antihypertensives derived from plants work in various ways, including reducing the volume of body fluids (diuresis), reducing peripheral resistance (vasodilators), or inhibiting the release of the hormone aldosterone. Most plants that have been found contain several compounds such as alkaloids, terpenoids, flavonoids, steroids, glycosides and saponins. But only a few have known the specific action of these plants in the treatment of hypertension (Loew & Kaszkin, 2002).

inggir-inggir fruit belongs to the genus Solanum is one of the medicinal plants that has the potential to be utilized as an antihypertensive drug. According to research by Thongpukdee, et al. (2010), it is known that inggir-inggir fruit is a medicinal plant commonly used to treat coughs and reduce blood glucose levels in diabetic patients. (Thongpukdee, A., dan Thepsitar, 2010). According to Fabellar (1998), regular consumption of inggir-inggir fruit can reduce blood glucose levels in diabetic patients. (Fabellar, 1998). Its use as an antihypertensive has not been widely studied but there are several cases in Indonesia, especially in North Sumatra, showing that consuming this plant can reduce high blood pressure. Although according to Maryono (2008), the use of medicinal plants as antihypertensives is not fully able to reduce blood pressure, but at least it can reduce the consumption of conventional drugs that are relatively expensive and reduce the side effects they cause. (Maryono, 2008). It is not yet known exactly the chemical content contained in inggir-inggir fruit but generally the solanaceae family has a high flavonoid content that has an effect as an antihypertensive. Solanum macrocarpum which also comes from the genus Solanum has been shown to have antihypertensive effects, and it is known that this plant contains a lot of bioflavonoids and monoterpenes (Iranloye et al., 2012). This suggests that most of the Solanum genus has antihypertensive activity.

According to research by Sinaga (2014), ethanol extract of inggir-inggir fruit at doses of 50, 100 and 150 mg/kg bw orally in male rats has a diuretic effect that is not statistically significantly different from furosemide at a dose of 3.6 mg/kg bw on sodium and potassium levels induced by 0.9% NaCl orally at a dose of 20 ml/kg bw. Therefore, this study tested the effect of ethanol extract of inggir-inggir fruit on reducing blood pressure in normotensive and hypertensive Wistar rats. (Sinaga, 2014)

2. METHOD

The objective of this study is to ascertain the influence of the independent variable on the dependent variable through an experimental approach. The study comprises the following stages: sample preparation, preparation of inggir-inggir fruit ethanol extract (EEBI), preparation of experimental animals, preparation of test materials, and testing the effect. A series of experiments will be conducted to test the effects of Inggir-inggir fruit ethanol extract on the blood pressure of rats with normal blood pressure, on the blood pressure of Wistar rats that have been made hypertensive, on the blood pressure of rats with hypertension that have been given the Inggir-inggir fruit ethanol extract, and on the data collected in each case. The effect of reducing BP was tested through non-invasive measurements of TDS, TDD, DJ, and TAR using the NIBP (Non-Invasive Blood Pressure) tool, as illustrated in Tables 3.1 and 3.2. The data from the study were analyzed with the SPSS 16.0 program using the ANOVA test.

The following tools were utilized in this study: laboratory glassware, porcelain cups, mortars and pestles, an analytical balance (Boeco), rat scales (Presica), an electric oven, a 27.5 G syringe (Terumo), a set of NIBP (non-invasive blood pressure) measuring devices (AD instrument), an oral sonde, a rat restrainer, and a warming lamp.

The plant material utilized in this investigation was the inggir-inggir fruit (Solanum sanctwongsei Craib.). The chemical constituents included CMC-Na (Merck), sodium chloride (Merck), deionized water, Tween 80, ultrasound gel (Ultra Sonography), methylprednisolone tablets (Dexa Medica), and bisoprolol tablets (Dexa Medica).

Sample collection and processing were conducted by Tri Ika Florida Sinaga (2014) in the study of the diuretic effect of an ethanol extract of Solanum sanctwongsei Craib. (inggir-inggir fruit) on male white rats. In this study, the same plant was utilized to avoid the need for repeated sample collection and processing. Sampling was conducted purposively, without comparison to specimens from other regions. Specimens were obtained from Buntu Bayu Village, Tanah Jawa District, Simalungun Regency, North Sumatra.

The preparation of extracts was conducted via maceration using a 96% ethanol solvent (DG POM, 1979). The extraction process was conducted by Tri Ika Florida Sinaga (2014) in their investigation of the diuretic effects of ethanol extracts derived from Solanum sanctwongsei Craib. in male white rats. In the present study, the same plant was utilized, thus eliminating the need for a second extraction process. The preparation method entails the following steps: The powder is placed into a sealed vessel, the liquid is poured until the entire simplisia is submerged and the vessel is closed, and the mixture is then left for five days. After this period, the mixture is blended, the pulp is macerated with 96% ethanol, and the resulting solution is stored in a sealed vessel and left in a cool place, protected from light for two days. Finally, the solution is poured. The methanol extract is concentrated using a rotary evaporator, resulting in a viscous solution (Directorate General of POM, 1979).

The animals utilized in this study were male white rats of the Wistar strain (Rattus norvegicus), weighing between 150 and 200 grams and aged between two and three months. Prior to the commencement of the study, the rats were maintained for a period of two weeks under identical environmental conditions, including food, temperature, and access to drinking water.

The preparation of materials includes the preparation of a 0.5% CMC Na suspension, a 2.5% NaCl solution, a methylprednisolone tablet suspension, an ingiger-inggir fruit ethanol extract suspension, and a bisoprolol tablet suspension.

The Labchart program should be opened on a computer that has been connected to the NIBP device. The parameters to be measured should then be set by clicking on the channel settings and adjusting the number of parameters to be measured. Channel 1 indicates the rat's TD electrical pulse, channel 2 denotes the NIBP device pump controller, and channel 3 represents the rat's heart rate. To calibrate the NIBP device, first locate the button

labeled "Start" at the end of the taskbar. Once pressed, the device will prompt the user to press the pump controller button. The pressure will subsequently increase to 300 mmHg on the sphygmomanometer. At the conclusion of the experiment, the "Stop" button should be selected if the pressure has decreased to 100 mmHg. The rat is then placed in the restrainer, and ultrasound gel is applied to the tail. The NIBP sensor and pump detector are then inserted into the rat's tail. Once the rat pulse has stabilized, the pump controller is pressed again. TDS and TDD can be observed on channel 1, while DJ can be seen on channel 3.

A total of 25 male Wistar rats were randomly assigned to one of five dose groups, one control group, one positive comparison group, and three test groups. Each group consisted of five male rats. The animals were grouped as follows:

Group I was administered a suspension preparation of CMC Na 0.5% (b/v).

Group II was administered a suspension preparation of inggigir fruit ethanol extract at a dose of 50 mg/kg bw.

Group II was administered a suspension preparation of inggir-inggir fruit ethanol extract at a dose of 100 mg/kg bb.

Group IV was administered a suspension preparation of inggir-inggir fruit ethanol extract at a dose of 150 mg/kg bb.

Group V was administered a suspension preparation of bisoprolol tablets at a dose of 0.0714 mg/kg bb.

Prior to the commencement of treatment, each group underwent initial BP measurement via the NIBP tool, administered via the tail vein. Each group was treated orally for seven consecutive days, after which BP measurement was repeated. Subsequently, treatment was continued for up to 14 days, with BP measurement occurring at the end of this period.

The results of this treatment will yield data on TDS, TDD, DJ, and TAR. TDS, TDD, and DJ can be obtained directly from the measurement results of the tool, while the TAR value is calculated using the formula outlined by (Shapiro, S, D., dan Loiacono, 2010) TAR is defined as follows: Once the TDS, TDD, DJ, and TAR have been obtained, the percentage decrease in BP of normotensive rats is then calculated using the formula provided by Siska et al. (2012) and Sanjaya (2010).

$$\% \text{ decrease in TD day X} = \frac{(\text{TD hari 0} - \text{TD hari x})}{\text{TD hari 0}} \times 100\%$$

A total of 30 Wistar male rats first measured their initial BP with NIBP device through the tail vein, then induced hypertension with 2.5% NaCl solution and a suspension of methylprednisolone tablets at a dose of 1.5 mg/kg bw every day for 7 consecutive days. Then the BP was measured again on the 7th day. Calculated the percentage increase in BP using the formula (Vogel, 2008), (Siska., Armenia., dan Arifin, 2011), (Sanjaya, 2010).

$$\% \text{ decrease TD hari X} = \frac{(\text{TD hari x} - \text{TD hari 0})}{\text{TD hari 0}} \times 100\%$$

A total of 30 hypertensive Wistar male rats that had been induced for 7 days were divided into 6 dose groups. 1 normal group (hypertension), 1 negative control group, 1 positive control group and 3 test groups. Each group consisted of 5 male rats. Animals were grouped as follows:

Group I: not given anything

Group II: given a suspension preparation of CMC Na 0.5% (b/v)

Group III: given a suspension preparation of inggir-inggir fruit ethanol extract at a dose of 50 mg / kg bw

Group IV: given a suspension of inggir-inggir fruit ethanol extract at a dose of 100 mg / kg bb

Group V: given a suspension preparation of inggir-inggir fruit ethanol extract at a dose of 150 mg / kg bb

Group VI: given a bisoprolol suspension preparation contained in tablets at a dose of 0.0714 mg / kg bb

The treatment was given every day until the 14th day. Rat BP was measured on the 8th, 9th, 10th, 11th, 12th, 13th and 14th days. Parameters measured include TDS, TDD, DJ and TAR. Then the percentage reduction in BP was calculated using the same formula in sub chapter 3.7.

The data were analyzed using the SPSS 16 program. The data were determined for homogeneity and normality to determine the statistical analysis used. Data were analyzed using ANOVA test to determine the average difference between groups. If there is a difference, it is continued with the LSD Post Hoc test to see the real difference between treatments.

3. RESULTS AND DISCUSSION

3.1 Raw Material Extract

In this research, the same ethanol extract of inggir-inggir fruit was used as the extract used by Tri Ika Florida Sinaga (2014) in a study entitled diuretic effect test of ethanol extract of nggir-inggir fruit (Solanum sanitwongsei

Craib.) on male white rats. Therefore, identification, phytochemical screening of samples and characterization are no longer carried out. The results of plant identification conducted at the Bogor LIPI Research and Development Center, showed that the plant under study was Solanum sanitwongsei Craib, can be seen in Appendix 1 page 84.

EEBI is stored in the refrigerator in a tightly closed container so that EEBI is protected from contamination of foreign substances. Storage in the refrigerator aims to prevent mold growth so as to prevent the extract from being exposed to direct sunlight. Organoleptically, the stored EEBI is not overgrown with mold and fungus. The ethanol extract of inggir-inggir fruit used is yellowish green in color, has a distinctive odor and bitter taste. The results of plant characterization and phytochemical screening can be seen in Tables 1 and 2.

Tabel 1. Characterization results of inggir-inggir fruit extracts

No	Parameter	Result (%)
1	Water content	6,65
2	Water soluble essence content	20,92
3	Ethanol soluble juice content	15,38
4	Total ash content	4,48
5	Acid insoluble ash content	0,43

Tabel 2. Phytochemical screening results of simplisia powder and ethanol extract of inggir-inggir fruit (EEBI) inggir-inggir (EEBI)

No	Parameter	Ingir-Inggir Fruit	
		Simplified powder	Ethanol extract
1	Alkaloida	+	+
2	Flavonoida	+	+
3	Saponin	+	+
4	Tannin	+	+
5	Glikosida	+	+
6	Steroida/Triterpenoida	+	+
7	Antrakuinon	-	-

Note: **+** = Make a result; **-** = Didn't make a result (Sinaga, 2014)

3.2 BP Decrease Test Results of Normotensive Rats

The results of the EEBI test on reducing BP in normotensive rats can be obtained from the measured parameters, namely the results of changes in TDS, TDD, DJ and TAR. Based on the results of statistical analysis of EEBI administration doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide a significant decrease in TDS ($p > 0.05$) against normotensive rats. The data obtained showed no significant difference in TDS ($p > 0.05$) on days 7 and 14 between treatment groups. Measurement on day 14, LSD results showed that the administration of EEBI doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide significant differences ($p > 0.05$) with the CMC-Na 0.5% group and the bisoprolol group as shown in Table 3.

The initial TDS of rats obtained was 132.32 ± 0.842 mmHg. Standard data for normal Wistar rat TDS has not been found but the TDS measured by Harwoko, et al., (2014) is ≤ 130 mmHg and according to Siska, et al., (2011), normal TDS is 139 mmHg. The difference in TD is likely influenced by the body weight of the rats and the physiological and environmental conditions of the rats.

Tabel 3 Mean TDS (mmHg) of normotensive rats day 0 before treatment, day 7 after treatment and day 14 after treatment

No	Group (N=5)	Average TDS (mmHg) hari 0±SD	Average TDS (mmHg) ±SD on the days	
			7	14
1	Normotensi + EEBI 50 mg/kg bb	134,4 ± 2,41	129,8 ± 6,5	127,8 ± 10,6
2	Normotensi + EEBI 100 mg/kg bb	132,8 ± 6,57	130,0 ± 3,7	123,2 ± 4,6
3	Normotensi + EEBI 150 mg/kg bb	132,6 ± 3,44	127,2 ± 4,3	122,8 ± 6,5
4	Normotensi + CMC-Na 0,5%	128,2 ± 3,77	125 ± 4,24	129,4 ± 3,8
5	Normotensi + SB 0,0714 mg/kg bb	133,6 ± 1,52	128,8 ± 4,2	126,2 ± 3,6

The average TDS on day 14 in the 50, 100 and 150 mg/kg bw test groups were 127.8 ± 10.64 mmHg, 123.2 ± 4.60 mmHg and 122.8 ± 6.49 mmHg respectively which were not significantly different (p> 0.05) with the negative control group. This indicates that EEBI cannot reduce the TDS of normotensive rats.

Data on the percentage of TDS reduction also showed no significant difference (p> 0.05) between treatment groups. The group that best reduces TDS is the EEBI group at a dose of 150 mg / kg bw which can only reduce TDS successively on days 7 and 14 is 4.01 ± 1.92% (5.4 mmHg) and 7.42 ± 1.42% (9.8 mmHg) but also not significantly different (p>0.05) with the control group as shown in Table 4. According to Thompson in Fidrianny (2003), the test substance is said to have an antihypertensive effect if it is able to reduce systolic blood pressure ≥ 20 mmHg. This shows that EEBI cannot reduce the TDS of normotensive rats.

Tabel 4 Mean percentage change in TDS (%) of normotensive rats on day 7 and day 14 after treatment

No	Group (N=5)	Percentage decrease in mean TDS (%)±SD on day	
		7	14
1	Normotensi +EEBI 50 mg/kg bb	3,39 ± 5,39	4,88 ± 8,15
2	Normotensi + EEBI 100 mg/kg bb	1,91 ± 5,64	6,99 ± 6,72
3	Normotensi + EEBI 150 mg/kg bb	4,01 ± 4,31	7,42 ± 3,13
4	Normotensi + CMCNa 0,5%	2,49 ± 1,29	0,60 ± 1,19
5	Normotensi + SB 0,0714 mg/kg bb	3,55 ± 4,21	5,52 ± 3,15

Based on the results of statistical analysis, the administration of EEBI dose of 50 mg/kg bw, EEBI dose of 100 mg/kg bw and EEBI dose of 150 mg/kg bw did not provide a significant decrease in TDD against normotensive rats. The average TDD of the whole group on days 0, 7 and 14 were 102.6 ± 3.571 mmHg, 96.96 ± 6.02 mmHg and 94.4 ± 6.59 mmHg respectively. Statistical analysis showed a significant difference (p < 0.05) in TDD on days 7 and 14 between treatment groups as shown in Table 5.

Tabel 5 Mean TDD (mmHg) of normotensive rats day 0 before treatment, day 7 and day 14 after treatment

No	Group (N=5)	Mean TDD (mmHg) day 0±SD	Mean TDD (mmHg) ±SD on day	
			7	14
1	Normotensi + EEBI 50 mg/kg bb	100,6 ± 4,56	99,2 ± 5,89	99,8 ± 10,28
2	Normotensi + EEBI 100 mg/kg bb	102,8 ± 2,86	93,4 ± 7,63	89,40 ± 3,85
3	Normotensi + EEBI 150 mg/kg bb	102,6 ± 1,52	92,2 ± 4,09	90,6 ± 3,05
4	Normotensi + CMC-Na 0,5%	101,6 ± 5,27	98,0 ± 3,16	95,0 ± 4,74
5	Normotensi + SB 0,0714 mg/kg bb	105,4 ± 1,14	102 ± 3,74	97,2 ± 3,56

The initial TDD of the rats obtained was 101.96 ± 3.846 mmHg. Standard data for normal Wistar rat TDD has not been found but according to Siska, et al., (2011), normal TDD is 119 mmHg and according to Iranloye, et al., (2011), normal TDD ranges between 96 ± 4.08 mmHg. This difference in BP may be influenced by the body weight of the rats and the physiological and environmental conditions of the rats.

Although there were significant differences (p < 0.05) between treatment groups, measurements on day 14 LSD results showed the administration of EEBI preparations at a dose of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide a significant difference (p> 0.05) with the control group (CMC-Na 0.5%) and bisoprolol group. This indicates that the administration of EEBI is not effective in reducing the TDD of normotensive rats.

Data on the percentage of TDD reduction also showed no significant difference (p> 0.05) between treatment groups on days 7 and 14. The group that best reduces TDD is the EEBI group at a dose of 150 mg / kg bw which can only reduce TDD respectively on days 7 and 14 is 10.15 ± 3.23% (8.6 mmHg) and 11.65 ± 3.94% (10.2 mmHg) but also not significantly different (p> 0.05) with the control group as shown in Table 6.

Tabel 6. Mean percentage change in TDD (%) of normotensive rats on day 7 and day 14 after treatment

No	Group (N=5)	percentage decrease in mean TDD (%)±SD on day	
		7	14
1	Normotensi + EEBI 50 mg/kg bb	3,52 ± 7,67	0,68 ± 10,49
2	Normotensi + EEBI 100 mg/kg bb	8,71 ± 7,85	12,98 ± 4,28

3	Normotensi + EEBI 150 mg/kg bb	10,15 ± 3,23	11,65 ± 3,94
4	Normotensi + CMC-Na 0,5%	3,35 ± 5,46	6,29 ± 6,64
5	Normotensi + SB 0,0714 mg/kg bb	3,22 ± 3,60	7,77 ± 3,50

According to Thompson in Fidrianny (2003), the test substance is said to have an antihypertensive effect if it can reduce BP ≥ 20 mmHg. This shows that EEBI doses of 50, 100 and 150 mg/kg bw cannot reduce the BP of normotensive rats.

Based on the results of statistical analysis, the DJ of rats was significantly different ($p < 0.05$) between groups before treatment. This is due to the unstable condition of the rats at the time of measurement. The administration of EEBI at a dose of 50 mg / kg bw, 100 mg / kg bw and a dose of 150 mg / kg bw did not provide a significant decrease in DJ against normotensive rats. The average DJ of the whole group on days 0 before treatment, 7 and 14 were 278.16 ± 105.84 BPM, 254.60 ± 110.9 BPM and 247.92 ± 105.07 BPM respectively. Statistical analysis showed no significant difference in DJ ($p > 0.05$) on days 7 and 14 between treatment groups as shown in Table 7.

Tabel 7. Mean DJ (BPM) of normotensive rats day 0 before treatment, day 7 and day 14 after treatment

No	Group (N=5)	Mean DJ (BPM) day 0 ± SD	Mean DJ (BPM) ± SD on day	
			7	14
1	Normotensi + EEBI 50 mg/kg bb	336 ± 44,49	275,6 ± 99,1	268,6 ± 44,6
2	Normotensi + EEBI 100 mg/kg bb	176,8 ± 105,1	157,6 ± 109	173,2 ± 109
3	Normotensi + EEBI 150 mg/kg bb	230,6 ± 119,2	225,8 ± 54,9	217,4 ± 119,28
4	Normotensi + CMC-Na 0,5%	281,0 ± 99,59	259,8 ± 98,2	273,6 ± 84,9
5	Normotensi + SB 0,0714 mg/kg bb	326,4 ± 21,56	354,2 ± 8,68	306,8 ± 90,6

From the data obtained, it can be seen that EEBI can reduce DJ in normal DJ but does not cause a significant decrease. The standard data of normal DJ of rats is still unknown. According to Iranloye, et al., (2011), the normal DJ of Sprague dawley rats is around 480 ± 35.54 BPM. According to Siska, et al. (2011), the normal DJ of Wistar rats is 344 BPM. This shows that there are clear differences in the DJ of Wistar rats based on dietary factors, body weight and also environmental or psychological factors at the time of measurement that cause an increase in DJ.

Measurement on day 14 LSD results showed the administration of EEBI doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide a significant difference ($p > 0.05$) with the control group and bisoprolol group.

Data on the percentage of DJ reduction also showed no significant difference ($p > 0.05$) between treatment groups on days 7 and 14. The test group that best reduces DJ is the EEBI group at a dose of 50 mg / kg bw which can only reduce DJ respectively on days 7 and 14 is 15.22 ± 38.05% (60.4 BPM) and 17.10 ± 39.06% (67.4 BPM) but also not significantly different ($p > 0.05$) with the control group (as shown in Table 8).

Tabel 8. Average percentage decrease in DJ (%) of normotensive rats on day 7 and day 14 after treatment

No	Group (N=5)	Percentage change in mean DJ (%) ± SD on day	
		7	14
1	Normotensi + EEBI 50 mg/kg bb	15,22 ± 38,05	17,10 ± 39,06
2	Normotensi + EEBI 100 mg/kg bb	9,72 ± 28,51	0,72 ± 24,17
3	Normotensi + EEBI 150 mg/kg bb	3,99 ± 10,42	4,59 ± 16,04
4	Normotensi + CMC-Na 0,5%	8,24 ± 4,41	0,61 ± 16,28
5	Normotensi + SB 0,0714 mg/kg bb	3,02 ± 8,51	16,24 ± 25,35

According to Siska, et al. (2011), the DJ of rats that have been induced by NaCl 2.5% and prednisone 1.5 mg/kg bw does not decrease significantly ($p > 0.05$) after giving celery root extract or captopril. This is due to the psychological condition of the rats at the time of measurement. Therefore, EEBI cannot reduce the DJ of normotensive rats.

Based on the results of statistical analysis of EEBI administration doses of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide a significant decrease in TAR (p> 0.05) against normotensive rats. Statistical analysis showed no significant difference (p> 0.05) TAR on day 7 and 14 between treatment groups as shown in Table 9.

Tabel 9. Mean TAR (mmHg) of normotensive rats day 0 before treatment, day 7 and day 14 after treatment

No	Kelompok (N=5)	rata-rata TAR (mmHg) hari 0 ± SD	rata-rata TAR (mmHg) ± SD pada hari	
			7	14
1	Normotensi + EEBI 50 mg/kg bb	111,6 ± 3,36	108,8 ± 5,63	108,8 ± 9,91
2	Normotensi + EEBI 100 mg/kg bb	112,4 ± 3,78	105,2 ± 5,12	100,2 ± 3,42
3	Normotensi + EEBI 150 mg/kg bb	112,2 ± 1,30	103,4 ± 5,31	101 ± 4,18
4	Normotensi + CMC-Na 0,5%	110,2 ± 4,27	106,6 ± 3,44	106 ± 3,94
5	Normotensi + SB 0,0714 mg/kg bb	114,6 ± 0,55	110,6 ± 2,70	106,4 ± 3,36

The mean TAR ± SD of the whole group on days 0, 7 and 14 were 112.2 ± 3.12 mmHg, 106.92 ± 4.65 mmHg, and 104.48 ± 6.09 mmHg, respectively. The initial TAR of the rats obtained was 112.2 ± 3.12 mmHg. Standard data for normal Wistar rat TAR has not been found but the TAR measured by Siska et al. (2011) was 129 mmHg and according to Yanti et al. (2010), normal rat TAR ranged from 73 ± 2.12 mmHg. The difference in TAR is likely influenced by the body weight of the rats and the physiological and environmental conditions of the rats.

Measurement on day 14, LSD results showed the administration of EEBI preparations at a dose of 50 mg / kg bw, 100 mg / kg bw and 150 mg / kg bw did not provide a significant difference (p> 0.05) with the control group and bisoprolol group. It can be seen that EEBI cannot reduce the TAR of normotensive rats.

Data on the percentage of TAR reduction also showed no significant difference (p> 0.05) between treatment groups. The group that best reduces TAR is the EEBI group at a dose of 100 mg / kg bw which can only reduce TDS successively on days 7 and 14 is 6.33 ± 5.28% (7.2 mmHg) and 10.72 ± 5.34% (12.2 mmHg) but also not significantly different from other treatment groups as shown in Table 10.

Tabel 10. Mean percentage change in TAR (%) of normotensive rats on day 7 and day 14 after treatment

No	Kelompok (N=5)	Rata-rata persentase penurunan TAR (%) ± SD pada hari	
		7	14
1	Normotensi +EEBI 50 mg/kg bb	2,41 ± 6,39	2,48 ± 8,85
2	Normotensi + EEBI 100 mg/kg bb	6,33 ± 5,29	10,72 ± 5,34
3	Normotensi + EEBI 150 mg/kg bb	7,85 ± 2,79	9,97 ± 3,38
4	Normotensi + CMC-Na 0,5%	3,19 ± 3,57	3,74 ± 3,91
5	Normotensi + SB 0,0714 mg/kg bb	3,48 ± 2,45	7,15 ± 2,98

According to Thompson in Fidrianny (2003), the test substance is said to have an antihypertensive effect if it can reduce TAR ≥ 20 mmHg. According to Iranloye, et al. (2011), water and ethanol extracts of Solanum macrocarpum which is also one genus with Solanum sanitwongsei can reduce TAR to 54 ± 5.59 mmHg and 49 ± 0.89 mmHg respectively in normotensive Sprague dawley rats. This shows that the genus Solanum generally has antihypertensive effects but when viewed based on research data the effect of Solanum macrocarpum is stronger than Solanum sanitwongsei in reducing BP in normotensive rats.

3.3 Results of BP Increase After Hypertension Induction

Based on the data obtained, the administration of 2.5% NaCl solution and methylprednisolone at a dose of 1.5 mg/kg bw for 7 consecutive days can significantly increase the TDS, TDD, DJ and TAR of normotensive rats ($p<0.05$) as shown in Table 11.

Tabel TD Results of hypertensive rats in each group after being induced with 2.5% NaCl solution and methylprednisolone at a dose of 1.5 mg/kg bw.

Group (N=6)	BP after 7 days of induction			
	TDS (mmHg)	TDD (mmHg)	DJ (BPM)	TAR (mmHg)
Hipertensi	192 ± 9,9	149,6 ± 5,5	385,4 ± 39,6	163 ± 4,9
Hipertensi + CMC-Na 0,5%	204 ± 9,4	160,6 ± 4,16	389,8±47,56	174,6 ± 4,1
Hipertensi + EEBI 50 mg/kg bb	269,8 ± 4,9	190,2 ± 10,4	392,4 ± 42,1	216,4 ± 6,9
Hipertensi + EEBI 100 mg/kg bb	201 ± 10,8	156,8 ± 4,9	385 ± 30,8	171,2 ± 5,2
Hipertensi + EEBI 150 mg/kg bb	194,4 ± 7,5	151,4 ± 5,8	390,4 ± 31,3	165,2 ± 1,8
Hipertensi + SB 0,0714 mg/kg bb	204,8 ± 7,9	163,2 ± 7,3	396,4 ± 43,4	176,8 ± 6,6

According to Siska, et al., (2011), the administration of 2.5% NaCl solution and prednisone at a dose of 1.5 mg/kg bw for 14 days to wistar rats can increase TDS, TDD, DJ and TAR respectively to 181 mmHg, 157 mmHg, 330 BPM and 170 mmHg. This shows a significant difference with the results of the study which may be due to differences in rats, environment and food given.

Data on the percentage increase in BP also showed that there were significant differences ($p < 0.05$) between treatment groups. The average increase in TDS, TDD, DJ and TAR of all groups was 59.60%, 84.23%, 27.93%, and 75.76% respectively as shown in Table 12.

Tabel 12 Mean percentage increase in BP (%) of hypertensive rats after induction of 2.5% NaCl and 1.5 mg/kg bw methylprednisolone

Group (N=6)	Mean percentage increase in BP (%) after 7 days of induction of hypertension			
	TDS (%)	TDD (%)	DJ (%)	TAR (%)
Hipertensi	46,7 ± 15,9	70,3 ± 30,4	43,8 ± 22,8	66,6 ± 25,9
Hipertensi + CMC-Na 0,5%	38,7 ± 7,2	68,5 ± 18,7	20,9 ± 16,9	58,4 ± 10,7
Hipertensi + EEBI 50 mg/kg bb	110,5 ± 19,7	116,7 ± 20,22	27,1 ± 14,4	113 ± 13,7
Hipertensi + EEBI 100 mg/kg bb	66,2 ± 12,3	102 ± 20,5	37,9 ± 11,7	86,7 ± 16,8
Hipertensi + EEBI 150 mg/kg bb	65,5 ± 15,7	108 ± 21,1	15,5 ± 10,9	92,2 ± 15,6
Hipertensi + SB 0,0714 mg/kg bb	30,1 ± 6,5	39,8 ± 9,4	22,4 ± 13,1	36,9 ± 6,8

According to Lailani, et al. (2013), giving 8% NaCl solution (8 ml/day) for 4 weeks can increase TDS, TDD, DJ, and TAR respectively to 191 ± 17 mmHg, 162 ± 17 mmHg, 317 ± 40 times per minute and 176 ± 17 mmHg. In the study of Ni and Vazri (2001) in Yanti, et al., (2010), high salt intake causes nitric oxide (NO) production in the kidney and vascular to decrease. NO is a potential endogenous vasodilator and plays a role in the regulation of vascular resistance. Methylprednisolone is a corticosteroid hormone compound with a sodium potency of 0.8%. The combination of methylprednisolone with NaCl will cause a retention effect sufficient to increase animal TD (Siska, et al., 2011).

3.4 BP Reduction Test Results of Hypertensive Rats

Testing the effect of reducing TD of hypertensive rats includes parameters of TDS, TDD, DJ and TAR on male white rats wistar strain. Based on the results of statistical analysis that the administration of the test preparation provides a significant decrease in TDS ($p < 0.05$) against hypertensive rats. Statistical analysis showed a significant difference ($p < 0.05$) TDS between treatment groups as shown in Table 13.

Tabel 13. Mean TDS (mmHg) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=6)	Mean TDS Day 7 ± SD	Mean Change TDS (mmHg) ± SD in days						
		8	9	10	11	12	13	14
Hipertensi	192,2 ± 9,88	191 ± 3,81	188 ± 5,79	190,4 ± 4,56	194 ± 5,43	194,2 ± 2,38	193,8 ± 1,92	190,8 ± 1,64
Hipertensi + CMC Na 0,5%	204 ± 9,35	195,8 ± 7,19	193,8 ± 6,91	197,6 ± 4,04	203,4 ± 10,74	192 ± 5,09	194,8 ± 1,79	194 ± 5,57
Hipertensi + EEBI 50 mg/kg bb	269,8 ± 4,87	268,4 ± 6,07	199,8 ± 10,38	186,2 ± 5,22	188,8 ± 3,35	185,4 ± 4,83	188 ± 2,83	185,4 ± 4,39
Hipertensi + EEBI 100 mg/kg bb	201 ± 10,84	184,8 ± 9,73	176 ± 3,61	172,8 ± 5,93	169 ± 4,85	175,4 ± 5,22	171,4 ± 6,47	167,2 ± 8,08
Hipertensi + EEBI 150 mg/kg bb	194,4 ± 7,47	184,6 ± 4,72	178,6 ± 5,68	178 ± 7,65	180 ± 7,45	177,6 ± 6,58	178,8 ± 4,49	173,8 ± 5,89
Hipertensi + SB 0,0714 mg/kg bb	204,8 ± 7,92	180 ± 8,43	173 ± 5,43	152,8 ± 4,44	151,4 ± 1,52	150,2 ± 1,92	145 ± 3,16	136,4 ± 3,36

The average initial TDS on day 7 of all groups of hypertensive rats obtained was 211.03 ± 28.25 mmHg. Standard data on the TDS of hypertensive wistar rats has not been found but the TDS of hypertension measured by Iranloye, et al., (2011) is 176.4 ± 7.38 mmHg and according to Siska, et al., (2011), the TDS of hypertensive wistar rats is 181 mmHg.

Measurement on day 14, LSD results showed the administration of EEBI dose of 100 mg/kg bw and dose of 150 mg/kg bw gave a significant difference ($p < 0.05$) with the normal group (hypertension). EEBI doses of 50 mg/kg bw, doses of 100 mg/kg bw and 150 mg/kg bw were also significantly different from the negative control group (CMC-Na 0.5%). The normal group and the negative control group did not have significant differences ($p > 0.05$) between the two groups. It can be seen that EEBI doses of 50 mg/kg bw, 100 mg/kg bw, and 150 mg/kg bw are more effective in reducing the TDS of hypertensive rats compared to the normal group without treatment and the negative control group given CMC-Na 0.5%.

Data on the percentage of TDS reduction also showed a significant difference ($p < 0.05$) between treatment groups. The test group proved to be able to reduce the TDS of hypertensive rats, namely EEBI doses of 50, 100 and 150 mg / kg b can reduce TDS successively to 30.09 ± 1.92% (84.4 mmHg), 16.45 ± 8.48% (33.8 mmHg) and 10.51 ± 4.21% (20.6 mmHg) as shown in Table 14.

Tabel 14 Average percentage change in TDS (%) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=5)	average percentage change in TDS (%) ± SD on day						
	8	9	10	11	12	13	14
Hipertensi	0,4 ± 5,4	2,0 ± 5,33	0,74 ± 5,28	-1,22 ±7,12	-1,26 ± 5,64	-0,99 ± 5,92	0,55 ± 4,41
Hipertensi + CMC Na 0,5%	4,01 ± 3,71	4,79 ± 6,43	2,96 ± 5,19	0,42 ± 8,46	5,72 ± 5,22	4,42 ± 4,46	4,68 ± 6,28
Hipertensi + EEBI 50 mg/kg bb	0,52 ± 1,25	25,91 ± 4,32	30,96 ± 2,56	30,00 ± 2,00	31,28 ± 1,45	30,28 ± 2,19	30,09 ± 1,92
Hipertensi + EEBI 100 mg/kg bb	7,68 ± 9,41	12,16 ± 6,49	13,75 ± 6,84	15,64 ± 6,65	12,47± 6,55	14,44 ± 6,94	16,45 ± 8,48
Hipertensi + EEBI 150 mg/kg bb	4,98 ± 2,83	8,06 ± 3,40	8,37 ± 4,22	7,28 ± 5,49	8,50 ± 5,49	7,88 ± 4,90	10,51 ± 4,21
Hipertensi + SB 0,0714 mg/kg bb	12,05 ± 2,98	15,48 ± 2,71	25,28 ± 3,36	25,98 ± 3,09	26,59 ± 2,48	29,08 ± 3,94	33,29 ± 3,83

Bisoprolol as a positive comparator was the group that best reduced the BP of hypertensive rats to 33.29 ± 3.83% (68.4 mmHg). According to Sanjaya (2010), bisoprolol can reduce TDS by 11.65% in Sprague dawley rats. This difference may be due to the type of rat, environment and food.

According to Thompson in Fidrianny (2003), the test substance is said to have an antihypertensive effect if it is able to reduce systolic pressure ≥ 20 mmHg. It can be seen that EEBI doses of 50, 100 and 150 mg/kg bw have an antihypertensive effect. According to Iranloye, et al. (2011), water and ethanol extracts of Solanum macrocarpum

which is also a genus of Solanum can reduce the TDS of hypertensive rats to 49 ± 3.46 mmHg and 57 ± 5.31 mmHg, respectively. This shows that EEBI is more effective in reducing BP in hypertensive rats.

Based on the results of statistical analysis, the administration of test preparations provides a significant decrease in TDD ($p < 0.05$) against hypertensive rats. Statistical analysis showed a significant difference ($p < 0.05$) TDD between treatment groups from day 8, 9, 10, 11, 12, 13 and 14 as shown in Table 15.

Tabel 15. Mean TDD (mmHg) of hypertensive rats on days 7 before treatment, 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=6)	mean TDD day 7 ± SD	mean change in TDD ± SD on day						
		8	9	10	11	12	13	14
Hipertensi	149,6 ± 5,46	152,8 ± 6,30	136,8 ± 8,08	150,8 ± 5,17	158,6 ± 7,02	163,4 ± 8,74	159,2 ± 1,48	153,4 ± 5,86
Hipertensi + CMC Na 0,5%	160,6 ± 4,16	158,2 ± 8,14	152,2 ± 3,56	157,4 ± 5,46	159,6 ± 7,86	158,8 ± 10,85	161,2 ± 3,63	154,6 ± 4,88
Hipertensi + EEBI 50 mg/kg bb	190,2 ± 10,38	192,4 ± 13,48	164,2 ± 3,11	141,6 ± 8,44	147,8 ± 6,38	161,8 ± 8,87	147 ± 6,00	153 ± 5,48
Hipertensi + EEBI 100 mg/kg bb	156,8 ± 4,97	142 ± 10,93	134,4 ± 2,79	129,4 ± 11,46	133,4 ± 3,36	137,6 ± 1,14	134,6 ± 3,64	131,8 ± 3,70
Hipertensi + EEBI 150 mg/kg bb	151,4 ± 5,81	142,8 ± 5,45	137,6 ± 5,32	137,6 ± 12,05	145,2 ± 2,28	150 ± 7,38	154,4 ± 1,52	130,6 ± 3,36
Hipertensi + SB 0,0714 mg/kg bb	163,2 ± 7,29	129,2 ± 7,29	128,4 ± 2,79	119,6 ± 3,84	122 ± 3,32	110,2 ± 6,54	108,8 ± 4,92	108,6 ± 6,54

The average initial TDD of all groups of hypertensive rats obtained was 161.97 ± 15.00 mmHg. Standard data on the TDD of hypertensive wistar rats has not been found but the TDD of hypertension measured by Iranloye, et al., (2011) is 131.6 ± 8.20 mmHg and according to Siska, et al., (2011), the TDD of hypertensive wistar rats is 157 mmHg.

Measurement on day 14, LSD results showed the administration of EEBI dose of 100 mg/kg bw and dose of 150 mg/kg bw gave a significant difference ($p < 0.05$) with the hypertension group (no treatment). EEBI doses of 100 mg / kg bw and 150 mg / kg bw were also significantly different ($p < 0.05$) with the negative control group (CMC-Na 0.5%). The normal group and the negative control group did not have significant differences ($p > 0.05$) between the two groups. It can be seen that the EEBI dose of 100 mg/kg bw, and the dose of 150 mg/kg bw are more effective in reducing the TDD of hypertension compared to the normal group and the negative control group.

Data on the percentage change in TDD of hypertensive rats also showed that there were significant differences ($p < 0.05$) between treatment groups. The test group is proven to reduce the TDD of hypertensive rats. EEBI group doses of 50, 100 and 150 mg/kg bw can reduce TDD successively to 19.31 ± 6.25% (37.2 mmHg), 15.88 ± 3.21% (25 mmHg) and 13.66 ± 3.25% (20.8 mmHg) as shown in Table 16.

Tabel 16 Average percentage change in TDD (%) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=5)	Mean percentage change in TDD (%) ± SD on day						
	8	9	10	11	12	13	14
Hipertensi	-2,27 ± 6,28	8,44 ± 6,68	-0,89 ± 4,60	-3,80 ± 3,23	-9,40 ± 8,06	-6,52) ± 3,90	-2,68 ± 6,21
Hipertensi + CMC Na 0,5%	1,45 ± 5,54	5,17 ± 3,68	1,91 ± 5,08	0,64 ± 3,62	1,08 ± 6,88	-0,42 ± 3,35	3,68 ± 4,03
Hipertensi + EEBI 50 mg/kg bb	-1,45 ± 9,9	13,48 ± 4,51	25,37 ± 5,99	21,98 ± 7,32	14,68 ± 7,46	22,46 ± 6,43	19,31 ± 6,25
Hipertensi + EEBI 100 mg/kg bb	9,35 ± 7,78	14,19 ± 3,81	17,48 ± 6,87	14,84 ± 3,97	12,18 ± 2,49	14,12 ± 2,25	15,88 ± 3,21
Hipertensi + EEBI 150 mg/kg bb	5,55 ± 5,70	7,92 ± 5,16	9,04 ± 8,11	3,99 ± 3,48	0,74 ± 7,47	-1,33 ± 4,74	13,66 ± 3,25
Hipertensi + SB 0,0714 mg/kg bb	20,73 ± 5,28	21,19 ± 4,16	26,61 ± 3,79	25,14 ± 3,71	32,38 ± 4,73	33,23 ± 4,08	33,67 ± 4,72

According to Thompson in Fidrianny (2003), the test substance is said to have an antihypertensive effect if it is able to reduce systolic pressure ≥ 20 mmHg. This indicates that EEBI has an antihypertensive effect. The difference in TD is likely influenced by rat strain, body weight, physiological conditions and rat environment.

According to Iranloye, et al. (2011), water and ethanol extracts of Solanum macrocarpum fruit which is also a genus of Solanum can reduce the TDD of hypertensive rats to 36.6 ± 3.57 mmHg and 35 ± 7.28 mmHg, respectively. This indicates that most of the Solanum genus has the effect of lowering TDD in hypertensive conditions.

Based on the results of statistical analysis of EEBI administration did not provide a significant decrease in DJ ($p > 0.05$) against hypertensive rats. Statistical analysis showed no significant difference ($p > 0.05$) in DJ reduction between treatment groups from day 8, 9, 10, 11, 12, 13 and 14 as shown in Table 17.

Tabel 17 Average DJ (BPM) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=6)	Mean DJ (BPM) day 7 ± SD	Mean change in DJ (BPM) ± SD on day						
		8	9	10	11	12	13	14
Hipertensi	385,4 ± 39,60	418,6 ± 13,83	448,8 ± 31,36	415,6 ± 11,26	370 ± 47,79	400,6 ± 47,93	342 ± 30,26	415 ± 42,38
Hipertensi + CMC Na 0,5%	389,8 ± 47,56	393,4 ± 29,95	388,6 ± 43,37	435,4 ± 20,35	410,8 ± 82,43	422,6 ± 50,32	375,2 ± 38,08	399,6 ± 63,08
Hipertensi + EEBI 50 mg/kg BB	392,4 ± 42,09	416,2 ± 16,48	371 ± 34,88	493,4 ± 15,92	416,6 ± 10,69	372,4 ± 28,88	409,2 ± 13,77	413,6 ± 41,72
Hipertensi + EEBI 100 mg/kg BB	385 ± 30,82	429 ± 41,66	454,4 ± 23,37	397 ± 73,96	426 ± 9,03	371,6 ± 30,34	397,4 ± 40,96	409,6 ± 26,33
Hipertensi + EEBI 150 mg/kg BB	390,4 ± 31,28	390,2 ± 42,72	374,6 ± 30,23	381,2 ± 44,26	400,6 ± 15,69	349 ± 16,16	426,2 ± 12,52	456,8 ± 30,43
Hipertensi + SB 0,0714 mg/kg BB	396,4 ± 43,43	426 ± 67,36	462,6 ± 22,05	372,6 ± 13,69	368,6 ± 7,79	377,4 ± 27,67	374,6 ± 29,69	461 ± 21,88

The average initial DJ of all groups of hypertensive rats obtained was 389.9 ± 36.261 mmHg. Standard data on the DJ of hypertensive wistar rats has not been found but the DJ of hypertensive rats given adrenaline injection measured by James, et al., (2011) was 343 ± 0.65 BPM and according to Siska, et al., (2011), the DJ of hypertensive wistar rats given 2.5% NaCl solution and 1.5 mg/kg bw prednisone for 2 weeks was 330 BPM.

Measurement on day 14, LSD results showed the administration of EEBI preparations at a dose of 50 mg / kg bw, a dose of 100 mg / kg bw and a dose of 150 mg / kg bw did not provide significant differences ($p > 0.05$) with the normal group (hypertension). EEBI dose of 50 mg/kg bw, and dose of 100 mg/kg bw also did not differ significantly ($p > 0.05$) with the negative control group (CMC-Na 0.5%).... The normal group and the negative control group did not have significant differences ($p > 0.05$) between the two groups.

Data on the percentage change in DJ also showed no significant difference ($p > 0.05$) between treatment groups. The test group could not reduce the DJ of hypertensive rats. The EEBI group doses of 50, 100 mg/kg bw and 150 mg/kg bw could not reduce DJ by -4.99 ± 22.09% (-21.2 mmHg), -6.46 ± 6.85% (-24.6 mmHg) and -17.67 ± 12.47% (-66.4 mmHg) respectively as shown in Table 18.

Tabel 18 Average percentage change in DJ (%) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=5)	Average percentage change in DJ (%) ± SD on day						
	8	9	10	11	12	13	14
Hipertensi	-9,31 ± 8,75	-17,78 ± 17,77	-10,58 ± 11,21	3,24 ± 15,29	-4,87 ± 16,17	10,72 ± 9,93	-8,86 ± 17,27
Hipertensi + CMC Na 0,5%	-2,09 ± 13,87	-1,03 ± 16,57	7,41 ± 17,29	14,59 ± 22,34	-9,57 ± 17,11	2,82 ± 13,84	-3,17 ± 16,76
Hipertensi + EEBI 50 mg/kg bb	-7,29 ± 14,92	3,87 ± 19,41	-26,88 ± 13,86	3,64 ± 14,89	3,79 ± 15,91	-5,05 ± 9,37	-4,99 ± 22,09
Hipertensi + EEBI 100 mg/kg bb	-11,9 ± 13,99	-18,59 ± 10,81	-3,62 ± 21,05	-11,17 ± 8,43	2,61 ± 14,26	-3.44 ± 9,77	-6,65 ± 6,85

Hipertensi + EEBI 150 mg/kg bb	-0,16 ± 10,45	3,55 ± 10,78	1,84 ± 13,41	-3,32 ± 11,59	10,21 ± 7,41	-9,79 ± 10,09	-17,67 ± 12,47
Hipertensi + SB 0,0714 mg/kg bb	-8,59 ± 22,69	-17,85 ± 13,92	5,00 ± 12,02	6,02 ± 11,30	4,11 ± 9,88	5,05 ± 7,85	-15,89 ± 11,71

Bisoprolol as a positive comparator also could not reduce the DJ of hypertensive rats by -15.89 ± 11.71% (-64.6 mmHg). According to Siska, et al. (2011), captopril which is also an antihypertensive drug cannot significantly reduce the DJ of hypertensive Wistar rats. This was due to the influence of the psychological condition of the rats when measuring BP. According to Iranloye, et al. (2011), water and ethanol extracts of Solanum macrocarpum fruit which is also a genus of Solanum can reduce the DJ of hypertensive rats to 286.4 ± 15.77 BPM and 272.8 ± 6.62 BPM, respectively. This suggests that most of the Solanum genus has the effect of lowering heart rate in hypertensive conditions but this study did not obtain these results. Previous research reported that EEBI has diuretic activity (Sinaga, 2014). It is suspected that this extract lowers blood pressure through a mechanism of decreasing peripheral resistance without causing a significant decrease in heart rate (Siska, et al., 2011).

Based on the results of statistical analysis, the administration of the test preparation gave a significant decrease in TAR ($p < 0.05$) to hypertensive rats. Statistical analysis showed a significant difference ($p < 0.05$) in TAR between treatment groups from day 8, 9, 10, 11, 12, 13 and 14 as shown in Table 19.

Tabel 19 Mean TAR (mmHg) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=6)	Mean TAR (mmHg) day 7 ± SD	Mean change in TAR (mmHg) ± SD on day						
		8	9	10	11	12	13	14
Hipertensi	163,2 ± 4,97	165,2 ± 3,96	153,6 ± 6,73	163,8 ± 3,56	170 ± 6,36	173,4 ± 5,41	170,4 ± 1,34	165,6 ± 4,09
Hipertensi + CMC Na 0,5%	174,6 ± 4,09	170,2 ± 6,65	165,6 ± 2,30	170 ± 4,12	173,6 ± 8,26	169,4 ± 7,50	172 ± 2,23	167,4 ± 2,07
Hipertensi + EEBI 50 mg/kg bb	216,4 ± 6,88	217,4 ± 9,53	175,8 ± 5,12	156,2 ± 6,46	161 ± 5,34	169,4 ± 7,23	160,2 ± 4,32	163,2 ± 4,97
Hipertensi + EEBI 100 mg/kg bb	171,2 ± 5,22	155,8 ± 10,52	148 ± 2,45	143,4 ± 8,71	144,8 ± 3,63	149,8 ± 2,28	146,6 ± 4,16	143,2 ± 2,17
Hipertensi + EEBI 150 mg/kg bb	165,2 ± 1,79	156,4 ± 4,83	150,8 ± 5,36	150,8 ± 8,76	156,4 ± 3,91	158,8 ± 5,98	162 ± 1,41	144,6 ± 3,05
Hipertensi + SB 0,0714 mg/kg bb	176,8 ± 6,61	145,8 ± 5,89	143 ± 1,87	130,4 ± 3,13	131,4 ± 2,07	123,2 ± 4,76	120,6 ± 3,58	117,2 ± 4,21

The average initial TAR of all groups of hypertensive rats obtained was 177.9 ± 18.79 mmHg. Standard data on the TAR of hypertensive wistar rats has not been found but the TAR of hypertensive Sprague dawley rats measured by Iranloye, et al., (2011) is 146.4 ± 7.58 mmHg and according to Siska, et al., (2011), the TAR of hypertensive wistar rats is 170 mmHg.

Measurement on day 14, LSD results showed that the administration of EEBI at a dose of 100 mg/kg bw and a dose of 150 mg/kg bw gave a significant difference ($p < 0.05$) with the normal group (hypertension) and the negative control group (CMC-Na 0.5%). The normal group and the negative control group (CMC-Na 0.5%) did not have a significant difference ($p > 0.05$) between the two groups.

Data on the percentage change in TAR of hypertensive rats also showed a significant difference ($p < 0.05$) between treatment groups. The test groups were proven to reduce the TAR of hypertensive rats. EEBI group doses of 50 mg/kg bw, 100 mg/kg bw and 150 mg/kg bw can reduce TDD successively to 24.49 ± 3.98% (53.2 mmHg), 16.28 ± 3.26% (28 mmHg) and 12.47 ± 1.36% (20.6 mmHg) as shown in Table 20.

Tabel 20 Average percentage reduction in TAR (%) of hypertensive rats on day 7 before treatment, day 8, 9, 10, 11, 12, 13 and 14 after treatment

Group (N=5)	Mean percentage change in TAR (%) ± SD on day						
	8	9	10	11	12	13	14
Hipertensi	-1,33 ± 4,60	5,86 ± 3,86	-0.40) ± 1,82	-4,21) ± 3,98	-3,89 ± 7,43	-4,37 ± 3,72	-1,55 ± 3,89

Hipertensi + CMC Na 0,5%	2,52 ± 3,18	5,25 ± 2,39	2,60 ± 2,66	0,57 ± 4,14	2,99 ± 3,04	1,77 ± 1,81	4,09 ± 1,56
Hipertensi + EEBI 50 mg/kg bb	-0,57 ± 6,18	18,70 ± 3,34	29,89 ± 5,81	25,49 ± 4,55	21,65 ± 4,41	25,88 ± 3,82	24,49 ± 3,98
Hipertensi + EEBI 100 mg/kg bb	8,59 ± 8,72	13,47 ± 3,72	16,15 ± 6,19	15,33 ± 4,27	12,42 ± 3,39	15,51 ± 3,97	16,28 ± 3,26
Hipertensi + EEBI 150 mg/kg bb	5,32 ± 3,11	8,69 ± 3,98	8,69 ± 5,58	5,34 ± 1,55	3,87 ± 3,45	1,93 ± 1,36	12,47 ± 1,36
Hipertensi + SB 0,074 mg/kg bb	17,48 ± 3,57	19,04 ± 2,89	26,72 ± 3,56	25,58 ± 3,38	30,27 ± 2,77	31,69 ± 3,57	33,64 ± 3,15

According to Iranloye, et al. (2011), water and ethanol extracts of Solanum macrocarpum fruit which is also a genus of Solanum can reduce the TAR of hypertensive rats to 41 ± 3.25 mmHg and 42.4 ± 6.42 mmHg, respectively. This shows that most of the Solanum genus has antihypertensive effects. Mean arterial blood pressure is much more important than systolic or diastolic pressure, because it is the mean arterial blood pressure that determines the mean velocity of blood flow in the systemic blood vessels (Guyton, 1993).

Based on the data obtained from testing the effect of lowering BP in normotensive and hypertensive rats, it can be seen that EEBI is more effective in lowering BP in hypertensive rats. This indicates that EEBI does not have a hypotensive effect on normal BP. Based on the research of Iranloye, et al., (2011), Solanum macrocarpum which is also the genus Solanum can cause hypotensive effects on normotensive and hypertensive Sprague Dawley rats. That is, the hypotensive effect of Solanum macrocarpum is stronger than Solanum sanitwongsei.

Active compounds that generally act as water-soluble antihypertensives are alkaloids and flavonoids while in the non-polar fraction are triterpenoids. According to Jaiswal (2012), some flavonoid compounds from Solanum torvum fruit have antihypertensive activity, namely rutin, quercetin, solagenin 6-β-D quinovopyranoside, solagenin 6-α-L ramnopiranosil. The mechanism of flavonoids as antihypertensive is known by inhibiting the release of angiotensin II from the renin-angiotensin system, inhibiting β-receptor activity in the heart and inhibiting calcium inflow (Agrawal, et al., 2010). Alkaloids and triterpenoids also contribute to lowering blood pressure. Some alkaloids isolated from Heimia salicifolia leaves have antihypertensive effects, namely lifolin, vertin and litrin. The mechanism of alkaloids in lowering blood pressure is thought to be through inhibition of angiotensin II in the renin system (Hernandez, et al., (2006). According to Harwoko, et al. (2014), the active compounds that play the most role as antihypertensives are triterpenoids. Asiaticosid, madekassosid, asiat acid and madesat acid are active compounds of the triterpenoid group that have antihypertensive effects (James and Dubery, 2011).

Solanum sanitwongsei also contains flavonoids, alkaloids and triterpenoids in its fruit (Sinaga, 2014). This shows that Solanum sanitwongsei has a good antihypertensive effect. The ability of various active compounds helps in treating hypertension which is also caused by various risk factors.

4. CONCLUSION

Based on the research that has been done, the conclusion of this study The results of statistical analysis show that the EEBI group doses of 50 mg / kg b, 100 mg / kg b and 150 mg / kg b are not significantly different ($p > 0.05$) with the control group (CMC-Na 0.5%) or the positive comparison group (bisoprolol) in reducing TDS, TDD, DJ and TAR normotensive Wistar rats. EEBI dose of 150 mg/kg bw is the test group that best reduces TDS, TDD and TAR of normotensive rats respectively, namely, 7.42 ± 1.42% (9.8 mmHg), 11.65 ± 3.94% (10.2 mmHg) and 9.97 ± 3.38% (10.1 mmHg). Meanwhile, the EEBI group at a dose of 50 mg/kg bw best reduced the DJ of normotensive rats, namely, 17.10 ± 39.06% (67.4 BPM). However, changes in BP in the test group did not differ significantly ($p > 0.05$) with the 0.5% CMC-Na control group which was also able to reduce TDS, TDD, DJ and TAR of normotensive rats respectively, namely, 0.60 ± 1.9% (3.2 mmHg), 6.29 ± 6.64% (6.6 mmHg), 0.61 ± 16.28% (8.2 BPM) and 3.74 ± 3.91% (3.6 mmHg). Therefore, EEBI could not reduce the BP of normotensive rats. The results of statistical analysis showed that EEBI doses of 50 mg/kg bw, 100 mg/kg bw and 150 mg/kg bw could significantly reduce TDS, TDD, and TAR of hypertensive wistar rats ($p < 0.05$) compared to the normal group without any administration and the CMC-Na 0.5% control group but could not significantly reduce DJ of hypertensive wistar rats ($p > 0.05$) with the normal group without any administration and the CMC-Na 0.5% group. EEBI dose of 50 mg/kg bw is the best group to reduce TDS, TDD and TAR of hypertensive rats respectively, namely, 30.09 ± 1.92% (84.4 mmHg), 19.31 ± 6.25% (37.2 mmHg) and 24.49 ± 3.98% (53.2 mmHg). EEBI doses of 50, 100 and 150 mg/kg bw were not effective in reducing the DJ of hypertensive rats respectively, namely, -4.99 ± 22.09% (-21.2 BPM), -6.46 ± 6.85% (-24.6 BPM) and -17.67 ± 12.47% (-66.4 BPM). Bisoprolol as a positive comparator also could not reduce the DJ of hypertensive rats, namely, -15.89 ± 11.71% (-64.6). This shows that the psychological condition of the animal greatly affects the DJ during measurement.

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