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Research Article

Comparison of blood pressure reduction between treatments of steeping red ginger rhizome (*Zingiber officinale* R.) and steeping binahong leaves (*Anredera cordifolia* (Ten.) Steenis) in healthy people with hypertension risk

Djelang Zainuddin Fickri[1]*, Arista Wahyu Ningsih[2], Martina Kurnia Rohmah[1], Khurin In Wahyuni[1], Novita E. Winarni[1], Pahri[1]
[1] Department of Clinical Pharmacy, High School of Health Sciences, Anwar Medika Hospital, Sidoarjo, East Java, Indonesia
[2] Department of Biologycal Pharmacy, High School of Health Sciences, Anwar Medika Hospital, Sidoarjo, East Java, Indonesia
* Corresponding Author's Email: fickri_farma@yahoo.co.id

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ABSTRACT

The potency of red ginger rhizome (*Zingiber officinale* R.) and binahong leaves (*Anredera cordifolia* (Ten.) Steenis) has been known to have an antihypertensive effect and can be used in herbal medicine. This study compared the impact of steeping red ginger rhizome and steeping binahong leaves on blood pressure reduction in healthy people with hypertension risk. The research design is a Comparative Quasy Experiment to measure pre-test and post-test blood pressure on treating 3 gr/200 ml steeping the red ginger rhizome (S1) and 3 gr/200 ml steeping binahong leaves (S2). The number of respondents was 64 according to the inclusion criteria and had obtained ethical clearance. The data were processed statistically. The experiment showed that the S1 group had a significant difference in systolic blood pressure reduction compared with the control treatments, but there was no significant difference in diastolic blood pressure reduction compared with controls. Meanwhile, in the S2 group, there was a significant difference in systolic blood pressure reduction compared with the control treatments, but there was no significant difference in diastolic blood pressure reduction compared with controls. Between the treatment of S1 and S2, there was no significant difference in systolic blood pressure reduction, which means that both red ginger and binahong seed had the same effect on systolic blood pressure. Treatment of steeping red ginger rhizome and steeping binahong leaves has a similar effect on systolic blood pressure reduction.

1. INTRODUCTION

Hypertension is defined as persistent blood pressure where the systolic and diastolic blood pressure is above 140/90 mmHg and above 160/90 mmHg in the elderly (Sheps, 2005). If hypertension can be controlled appropriately, it can reduce the risk of death, cardiovascular disease, stroke, and heart failure (Yonata & Pratama, 2016). According to WHO data, approximately 26.4% of the world's population has hypertension, and it will likely continue to increase to 29.2% in 2025 if the condition of the people's lifestyle is not controlled (Park, Kario & Wang, 2015). Hypertension is a progressive disease and has become a major global health problem. Of the 972 million people with hypertension, 333 million are in developed countries, and 639 million are in developing countries, including Indonesia (Yonata & Pratama, 2016). In general, the management of hypertension is pharmacological and non-pharmacological. Pharmacological therapy includes chemical and herbal medicines. Pharmacological treatment with chemical drugs has adverse effects, such as using thiazide-type diuretics in hypertensive patients accompanied by hyperuricemia can lead to joint inflammation. Hypertensive patients with a history of asthma should avoid β-blocker as they can aggravate asthmatic conditions (Pusat Data dan Informasi Kementrian Kesehatan RI [PUSDATIN KEMENKES RI], 2014). So, it is necessary to develop the potential treatment from natural ingredients because it has minimal side effects.

Alternative hypertension treatment from natural ingredients, for example, is red ginger and binahong (Kikuzaki & Nakatani, 1993; Duke, Bogenschutz-Godwin, duCellier & Duke, 2002). The potency of the red ginger rhizome (*Zingiber officinale* R.) and binahong leaves (*Anredera cordifolia* (Ten.) Steenis) has been known to have an antihypertensive effect and can be used in herbal medicine. In previous studies, the antihypertensive effect of 70% ethanol extract from red ginger was tested, which significantly affected systolic blood pressure reduction compared with negative controls, and the highest systolic blood pressure reduction was 27.35% in rats (Rahmah, 2008).

The main bioactive compounds in red ginger are 4-diarylheptanoid, shogaol, gingerol, and gingeron, with higher antioxidant activity than vitamin E (Zakaria & Rajab, 1999). In another in vivo test, red ginger has antihypertensive activity in salt-induced mice for five weeks (Mohan, Blalaraman & Kasture, 2007). Gingerol is known to reduce blood pressure systemically in mice at doses 10-100 μg/kg and cause bradycardia when given intravenously (Suekawa et al., 1984; Suekawa, Aburada, & Hosoya, 1986). Other studies have shown that gingerol in ginger has an anticoagulant effect, which prevents blood clots, thereby preventing blockage of blood vessels, which is the leading cause of strokes and heart attacks (Masuda, Kikuzaki, Hisamoto & Nakatani, 2004). (6)-shogaol, (6)-gingerol, and (10)-gingerol have antioxidant effects (Ghayur & Gilani, 2005). Antioxidants can reduce free radicals such as superoxide anion, thromboxane A2, endothelin, and endoperoxides which can cause hypertension. Superoxide anions can reduce nitric oxide. While thromboxane A2, endothelins, and endoperoxides trigger factors endothelial vasoconstriction. Antioxidants also can increase nitric oxide (NO) (Kojšová et al., 2006). Nitric oxide (NO) causes vasodilation effects (Katzung, Masters & Trevor, 2014). Total Peripheral Resistance (TPR) decreases at the time of vasodilation, resulting in lower blood pressure. Flavonoids have an inhibitory effect that prevents the angiotensin-converting enzyme (ACE) (Dipiro, Wells, Schwinghammer & Dipiro, 2012). Flavonoid prevents ACE activity, causing vasodilation, decreasing cardiac output, and ultimately decreasing blood pressure (Gray, Dawkins, Morgan & Simpson, 2005).

Binahong leaves are empirically often used routinely as many as nine pieces every day to lower blood pressure. The research results by Astuti, Sakinah, Andayani and Risch (2011), showed that binahong leaves contain flavonoids, alkaloids, saponins, steroids, triterpenoids, and polyphenols. The flavonoid content in fresh samples of binahong leaves was 11.23 mg/kg and 7.81 mg/kg (Rachmawati, 2009). In other research binahong leaveshave averaged 1.08% of saponins, 1.58% of tannins, and 0.39% of flavonoids (Sari, 2006). The flavonoids in binahong leaves allow the plant to be used to reduce blood pressure. Flavonoids may inhibit ACE, inhibiting the conversion of angiotensin I to angiotensin II and decreasing antidiuretic hormone secretion. As a result, much urine is excreted, and eventually, the blood pressure decreases (Widiasari, 2018). The type of flavonoids compounds in extracts binahong is flavonols. These compounds can eliminate oxidative stress, inhibit the angiotensin-converting enzyme (ACE) activity, improve endothelial relaxation of blood vessels, and regulate cell signaling and gene expression. Flavonols act as major antioxidants in biological systems. Flavonols show potential as an ACE inhibitor in vitro and in vivo, the ethanol extract of binahong leaves is effective in reducing the blood pressure of male Wistar rats at a dose of 50 mg /kg BW ($p = 0.05$) and a dose of 100 mg/kg BW ($p = 0.002$) (Aidasari, 2018). According to research by Siswantari (2011), giving binahong leaves boiled water can lower blood pressure in the elderly.

Both of these herbal ingredients have active compounds believed to be antihypertensive with almost the exact vasodilator mechanism. Necessary to study both the herbal ingredient if administered in the form of steeping water. The effect of lowering blood pressure was assessed as a direct response to the administration of steeping the red ginger rhizome and steeping binahong leaves.

2. MATERIALS AND METHODS

Research Design

The research design is a Comparative Quasy Experiment to measure the pre-test and post-test blood pressure on the treatment of 3 gr/200 ml steeping the red ginger rhizome and 3 gr/200 ml steeping binahong leaves, measuring pre-test and post-test with a range of four hours. Both groups were observed before treatment, then observed again after treatment. Subjects were observed in blood pressure (pre-test), then given treatment in the group of red ginger (S1), and the group leaves binahong (S2), then observed to measure blood pressure (post-test) after four hours. The independent variable was the treatment of steeping the red ginger rhizome 3 gr/200 ml, and binahong steeping leaves 3 gr/200 ml, and the dependent variable is blood pressure value.

Population and Sample

Population in the study were people in Desa Bungkeng, Kecamatan Tanjung Bumi, Kabupaten Bangkalan who were given steeping S1 and people in Desa Gempol Kurung, Kecamatan Menganti, Kabupaten Gresik who were given S2. The number of samples was determined by the Lameshow formula and using a non-random purposive sampling method. Samples according to the inclusion and exclusion criteria of the study.

The inclusion criteria in this study included over 25 years of age, obesity (BMI > 25), smokers, excessive caffeine consumption, excess salt consumption. The exclusion criteria included having a history of allergies to steeping binahong leaves and steeping red ginger, disliking steeping red ginger and binahong steeping, taking hypertension drugs or other drugs.

Treatment Preparation

The process of steeping red ginger rhizome and steeping binahong leaves is as follows clean the red ginger and binahong leaves first. After washing, it is chopped small and dried by peeling it at room temperature. After that, it is crushed into powder. 3 gr of dry red ginger powder are put into a tea pouch. By the same token with binahong leaves powder. Then steeped with 200 ml hot water at 900 ^{o}C until the color change and let stand for two minutes. The same procedure was applied to binahong leaves powder.

Preparing a placebo is the same as the method above and filling it with 3 gr small chunks of tea pouch and put into the tea pouch. Then steeped with 200 ml hot water at 900 ^{o}C until the color change and let stand for two minutes.

Data Analysis Method

The data were analyzed using the SPSS 22.0 program. Data were tested for normality with a significance level of a = 0.05. Paired T-test was performed to test the differences in each group on parametric data, and the Wilcoxon test on non-parametric data with a significance level of a = 0.05. The comparison test used the Mann-Whitney test with a significance level of a = 0.05.

Ethical Approval

The research design carefully studied research involving healthy people and compliance with all relevant national regulations and institutional policies with Faculty of Dental Medicine Health Research Ethical Clearance Commission (Faculty of Dental Medicine, Universitas Airlangga, Surabaya, Indonesia). The Research protocol was declared to be ethically appropriate and receiving certified (100/HRECC.FODM/III/2020 & 196/HRECC.FODM/IV/2020) for the care and use of human subjects.

3. RESULTS AND DISCUSSIONS

Result

Characteristics of the respondents are presented in the **Table 1**. The number of respondents was 64 people consisting of two groups from different locations, from Desa Bungkeng (S1) and Desa Gempol Kurung (S2), and each of these groups had two treatment groups with the same individual being a negative control group and treatment group. In the negative control group, respondents were given placebo intervention, while in the treatment group, the respondents were given steeping red ginger (S1) and steeping binahong leaves (S2).

Table 1. Respondent characteristics

Category	S1[1]		S2[2]	
Gender				
- Male	17	53%	12	37,5%
- Female	15	47%	20	62,5%
N	32	100%	32	100%
Age				
- 25-35 years	13	40%	15	46,9%
- 36-45 years	6	19%	14	43,7%
- 46-55 years	8	25%	3	9,4%
- 56-65 years	5	16%		
N	32	100%	32	100%
Jon				
- private employees	8	25%	12	37,5%
- entrepreneur	2	6%	5	15,6%
- housewife	7	22%	11	34,4%
- farmer	15	47%	4	12,5%
N	32	100%	32	100%

[1]S1 : People in Desa Bungkeng, Kecamatan Tanjung Bumi, Kabupaten Bangkalan who were given steeping red ginger rhizome
[2]S2 : People in Desa Gempol Kurung, Kecamatan Menganti, Kabupaten Gresik who were given steeping binahong leaves

Table 2. Pre-test and post-test blood pressure value in the control groups

Group	Variable		N	Maks	Min	Mean ± SD	P
Control (S1)	Systolik	Pre-test	32	214	101	140 ± 27	0,620
		Post-test	32	212	102	141 ± 26	
	Diastolic	Pre-test	32	144	60	90 ± 17	0,092
		Post-test	32	142	67	92 ± 16	
Control (S2)	Systolic	Pre-test	32	157	131	144 ± 7	0,720
		Post-test	32	156	130	142 ± 8	
	Diastolic	Pre-test	32	96	85	92 ± 3	0,600
		Post-test	32	94	81	90 ± 3	

Table 3. Pre-test and post-test blood pressure value in the treatment groups

Group	Variable		N	Maks	Min	Mean ± SD	P
S1	Systolic	Pre-test	32	199	99	141 ± 27	0,000
		Post-test	32	182	100	134 ± 16	
	Diastolic	Pre-test	32	148	65	91 ± 24	0,000
		Post-test	32	143	62	87 ± 17	
S2	Systolic	Pre-test	32	162	133	148 ± 8	0,000
		Post-test	32	156	123	142 ± 8	
	Diastolic	Pre-test	32	100	80	92 ± 3	0,000
		Post-test	32	100	80	90 ± 3	

Table 4. Blood pressure reduction value and compared with controls

Group	Variable		N	Maks	Min	Mean ± SD	P
S1	Systolic	Control	32	5	2	3,23 ± 1,23	0,001
		Treatment	32	8	1	4,32 ± 1,08	
	Diastolic	Control	32	6	3	3,24 ± 1,43	0,097
		Treatment	32	9	3	5,43 ± 1,78	
S2	Systolic	Control	32	5	1	2,44 ± 1,24	0,000
		Treatment	32	10	2	5,25 ± 1,95	
	Diastolic	Control	32	4	0	1,44 ± 1,08	0,512
		Treatment	32	5	0	1,75 ± 1,49	

Table 5. Comparison of Blood Pressure Reduction Value of S1 and S2 Respondents

Variable	Mean ± SD		P
	S1	S2	
Systolic	4,32 ± 1,08	5,25 ± 1,95	0,078
Diastolic	5,43 ± 1,78	1,75 ± 1,49	0,000

Description of data will show mean value, standard deviation, maximum and minimum value. Description of data are shown in **Table 2**, **Table 3**, **Table 4**, and **Table 5**.

Discussion

All respondents did not have a history of hypertension diagnosis and look healthy even though most respondents had high blood pressure. Men are more susceptible to hypertension because of a worse lifestyle by smoking and drinking coffee which can cause increase blood pressure due to the nicotine in cigarettes and caffeine in coffee. The risk of hypertension increases with age. It is caused by changes in the structure and function of the peripheral vascular system responsible for changes in blood pressure. These changes include the formation of atherosclerosis, loss of fibroblast elasticity, and decreased smooth muscle relaxation. As a result, the aorta and arteries decrease in stretch and reduce the capacity to accommodate blood volume from the heart. Then lead to an increase in cardiac output and peripheral resistance so blood pressure will rise (Dipiro et al., 2012; Gray et al., 2005).

Pressure and stressful job demands can stimulate the release of adrenal hormones and trigger the heart to beat faster so that the blood pressure will rise. Anxiety at work will affect sympathetic nerve activity, and vasoconstriction occurs. Vasoconstriction resulting in renal blood flow down and can cause renin release. Renin stimulates the formation of angiotensin I, which is then converted into angiotensin II. This hormone causes sodium and water retention in the renal tubules so that intravascular pressure increases and increases blood pressure (Dipiro et al., 2012; Gray et al., 2005. Respondents rarely felt the symptoms of hypertension in direct interviews.

Sodium intake, stress, obesity, genetics can affect cardiac output and peripheral resistance. Blood pressure will increase if there are abnormalities in these factors and result in changes in the aorta walls and blood vessels. Furthermore, the systolic blood pressure rises with no or minor diastolic changes. Increased systolic blood pressure causes the heart workload to become heavier, and eventually, the left ventricle walls thicken due to adaptation. Initially, the thickening of the verticle wall is for transformation, over time, will increase heart workload and become a pathological condition. When the heart workload increases, the heart will pump blood faster, and blood pressure will rise.

In this study, all-male respondents had the habit of smoking and drinking coffee, and almost all of the female respondents had a salty appetite or high sodium consumption, which resulted in high blood pressure (**Table 1**). Excess salt intake can cause fluid buildup in the body because it attracts extracellular fluid, which increases blood volume and pressure. This result proves that the respondent's food intake will affect blood pressure. The smoking habit will damage the endothelial lining of blood vessels due to nicotine and carbon monoxide from cigarettes, which then triggers the atherosclerosis process and blocks the supply of oxygen and nutrients to organs, especially the heart. Atherosclerosis will increase cardiac output and blood pressure (PUSDATIN KEMENKES RI, 2014). While at the coffee drinking habits with the most considerable caffeine content will bind adenosine receptors, activate the sympathetic nervous system by increasing concentrations of catecholamines in plasma, and increase cortisol production. It impacts vasoconstriction and increases total peripheral resistance, which will cause an increase in blood pressure (Dipiro et al., 2012; Gray et al., 2005).

The control group S1 respondents as many as 20 respondents observed a decrease in systolic pressure, and 23 respondents observed a reduction in diastolic blood pressure, which means that giving placebo did not provide a significant change in blood pressure (**Table 2**). While the treatment group of 30 respondents observed a decrease in systolic pressure and 28 respondents observed a decrease in diastolic blood pressure, which means that the treatment of steeping red ginger gives a significant change in blood pressure (**Table 3**).

Red ginger has benefits in the cardiovascular system. Red Ginger has antioxidant effects that reduce free radicals and blood pressure through calcium channel blockade (Ghayur & Gilani, 2005). Red ginger can also cause a decrease in blood pressure by inhibiting ACE activation (Ghayur, Gilani, Afridi & Houghton, 2005). Red ginger contains flavonoids, saponins, and non-flavonoid phenols. Flavonoids have an inhibitory effect on angiotensin-converting enzyme (ACE) activity which reduces the formation of angiotensin II from angiotensin I, which results in vasodilation, reduces cardiac output, and finally reduces blood pressure (Dipiro et al., 2012; Gray et al., 2005). Inhibition of ACE can also increase nitric oxide and decrease superoxide anions, causing vasodilation (Kojšová, et al., 2006). Red ginger also contains phenolic compounds such as (6)-shogaol and (6)-

gingerol, (10)-gingerol, which have antioxidant effects (Ghayur & Gilani, 2005). Antioxidants can reduce free radicals such as thromboxane A2, endothelins, and endoperoxides, endothelial vasoconstriction factors (Kojšová et al., 2006; Dipiro et al., 2012). In addition, red ginger also contains saponins that inhibit renin (RAA system) in the kidneys (Dipiro et al., 2012; Gray et al., 2005). So that reduces the formation of angiotensin II and reduces aldosterone secretion, which causes an increase in excretion of salt and water by the kidneys and causes a decrease in cardiac output (Gray et al., 2005).

When there is too much salt and water in the body, blood pressure increases utilizing a complex physiological mechanism that alters venous return to the heart, causing an increase in cardiac output. Pathological conditions that change renal threshold will increase systemic arterial pressure. Renin and angiotensin play a role in regulating blood pressure. Kidneys produce renin, an enzyme on the plasma protein substrate to secrete angiotensin I, converted by the angiotensin-converting enzyme into angiotensin II and then angiotensin III. Angiotensin II and III are potent vasoconstrictors of blood vessels and control the release mechanism of primary aldosteronism. Angiotensin II and III inhibitory effects on sodium excretion (Dipiro et al., 2012; Gray et al., 2005). Researchers argue that red ginger compounds lead to a tool for lowering blood pressure in the vascular system (peripheral resistance) as a vasodilator. They have decreased peripheral resistance due to dilation of blood vessels, resulting in a decrease in systolic pressure without reducing diastolic pressure. There is no decrease in fluid (cardiac output) related to the mechanism of cardiac performance at diastolic pressure.

In S2 respondents, the control group, all respondents observed a decrease in systolic pressure, and 25 respondents observed a reduction in diastolic blood pressure, which means that giving placebo did not provide a significant change in blood pressure (**Table 2**). While the treatment group of all respondents observed a decrease in systolic pressure and 22 respondents observed a decrease in diastolic blood pressure, which means that the treatment of steeping binahong leaves gives a significant change in blood pressure (**Table 3**).

The flavonoids in binahong leaves are flavonols. These compounds can reduce oxidative stress, inhibit ACE activity, and increase the relaxation of blood vessel endothelium (Aidasari, 2018). Flavonoids inhibit the conversion of angiotensin I to angiotensin II, causing vasodilatation. Flavonoids, like ACE inhibitors, can also impede aldosterone secretion from the adrenal cortex causes NaCl excretion will increase, and finally, blood pressure will decrease (Widiasari, 2018). The difference in systolic and diastolic pressure results is due to the flavonoid content in binahong leaves, which acts as an ACE inhibitor that can improve arterial compliance and distensibility. This role can cause a decrease in systolic pressure that is more significant than diastolic (Ghayur et al., 2005). Researchers argue that the flavonoid mechanism, in this case, flavonol, in addition to providing a vasodilating effect, must also affect NaCl excretion through the RAAS system in the kidneys by inhibiting aldosterone secretion from the adrenal cortex, thereby reducing cardiac preload, in this case, it can be seen from the value diastolic. However, the results of this study did not show a significant decrease in the diastolic value, this may be because the amount of fluid that the respondent drank during the measurement process between the pre-test and post-test could not be controlled. These are the limitations and weaknesses of this study. So, it is necessary to do further research related to the mechanism of reducing blood pressure from steeping binahong leaves by adding urine parameters to assess the amount of fluid in each treatment condition.

4. CONCLUSIONS

Treatment of steeping red ginger rhizome (*Zingiber officinale* R.) and steeping binahong leaves (*Anredera cordifolia* (Ten.) Steenis) has a similar effect on systolic blood pressure reduction.

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