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Research Article

Diuretic Potency of *Belalai Gajah* Plants (*Clinacanthus nutans* (Burm.fil.) Lindau)

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ABSTRACT

Backgrounds: The use of *belalai gajah* plants (*Clinacanthus nutans* (Burm.fil.) Lindau) is believed by the Chinese community to be able to treat hypertension, so to prove whether this power exists in *belalai gajah* plants is to do a diuretic activity test. **Objective of Study:** to determine the presence of diuretic potency in *belalai gajah* plants. **Methods:** This test used male white rats of the Sprague Dawley strain with a body weight of 200-250 grams aged 2-2.5 months as many as 35 rats which were divided into 7 groups. The first group or no treatment, the second group with 2.8 ml/200 g body weight of distilled water, the third and fourth groups with 0.72 mg/200 g body weight of furosemide and 1.44 mg/200 g body weight, the fifth, sixth, and seventh groups with administration of *belalai gajah* plants extract doses of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight. This test uses the Cumming method. Urine collection was carried out for 24 hours, then urine volume, urine pH, also sodium and potassium levels in rat urine were measured. **Results:** The results of this study showed that without treatment, the administration of distilled water at a dose of 2.8 ml/200 g body weight, furosemide at a dose of 0.72 mg/200 g body weight and 1.44 mg/200 g body weight, and *belalai gajah* plants extract at a dose of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight resulted in a urine volume of 13.01 ± 0.07 ml; 13.77±0.17 ml; 15.78± 0.39 ml; 18.13±0.23 ml; 14.05±0.06 ml; 16.78±0.12 ml; 17.98±0.09 ml ($p<0.5$). Furthermore, the urine pH was successively 7.02 ± 0.04; 7.11±0.02; 7.21±0.02; 7.58±0.18; 7.15±0.03; 7.37±0.03; 7.44±0.02 ($p>0.5$). The results of sodium levels in urine were respectively 1.06±0.03 mEq/ml; 1.14±0.03 mEq/ml; 2.17±0.09 mEq/ml; 4.01±0.069 mEq/ml; 1.34±0.08 mEq/ml; 1.49±0.02mEq/ml; 1.77 ±0.05 mEq/ml ($p<0.5$) and urinary potassium levels 0.5±0.03 mEq/ml, respectively; 0.57±0.018 mEq/ml; 0.98±0.023 mEq/ml; 1.88±0.04 mEq/ml; 0.6±0.02 mEq/ml; 0.76±0.021 mEq/ml; 0.87±0.032 mEq/ml ($p<0.5$). **Conclusion:** *Belalai gajah* plants extract at a dose of 300 mg/kg body weight has the ability to increase urine volume which is close to the urine volume by administering furosemide 1.44 mg/200 g body weight. *Belalai gajah* plants extract at a dose of 75 mg/kg body weight had a urine pH close to urine pH by administering distilled water at a dose of 2.8 ml/200 g body weight and 0.72 mg furosemide/200 g body weight. Giving *belalai gajah* plants extract at a dose of 75 mg/kg body weight has potassium levels in the urine that are close to urine potassium levels by administering distilled water.

Key words: *Clinacanthus nutans* (Burm.fil.) Lindau, Diuretic Potency, Urine.

BACKGROUNDS

Hypertension is a major risk factor for cardiovascular disease and chronic kidney disease, the leading cause of death globally.[1] Hypertension or high blood pressure is a condition where after two separate measurements there is an increase in systolic blood pressure ≥140 mmHg and/or diastolic ≥90 mmHg.[2-4] If left unchecked, this disease can interfere with the function of other organs such as the heart and kidneys which are vital organs.[5] Symptoms that can be caused in people with hypertension are chest pain, vision problems, ringing in the ears, fatigue, confusion, headache, feeling of heaviness in the back of the neck, vertigo, nosebleeds, dyspnea/ shortness of breath, increased frequency of urine, nausea, sleep apnea, irregular heartbeat regular.[6,7] Factors that cause hypertension are age, family history, being overweight/obese, not being physically active, using tobacco, consuming too much salt (sodium) in the food consumed, too little potassium in the food consumed, consuming too much alcohol.[8] Hypertension often occurs in patients with chronic kidney disease. Hypertension management is needed to control blood pressure and prevent complications. Prevention of hypertension can be done with non-pharmacological efforts such as weight loss and limiting salt intake. As for pharmacological treatment such as therapy with antihypertensive drugs, one of which is diuretics.[7] Diuretics are drugs that can increase urine production due to the excretion of water and electrolytes by the kidneys.[10,11] The accumulation of fluid in the body's tissues is due to the inability of the kidneys to release sodium and water which are excreted together. Diuretics can be used to treat edema, heart failuure, and hypertension.[11] Diuretics can be categorized into three groups: loop diuretics, thiazide diuretics, and potassium-sparing diuretics.[12-14]

Diuretics are used to improve the composition and volume of fluids in the body, which treats hypertension.[15,16] The mechanism of action of diuretic drugs in lowering blood pressure is by helping the kidneys function in filtering, removing salt and water, which in turn reduces the volume of fluids in the body so that blood pressure also decreases.[7,17] Hypertension is generally treated using synthetic drugs such as furosemide.[18-21] Furosemide is a loop diuretic that can reduce the reabsorption of sodium produced by the kidneys. Furosemide can inhibit the luminal Na-K-Cl co-transporter in the loop of Henle by binding to the chloride transport channel. In this case, elevated levels of Na, Cl, and K remain in the urine.[22] Long-term use of furosemide is known to cause electrolyte balance disturbances (excessive loss of sodium and potassium),

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volume depletion so that it may cause arrhythmic heart attacks and hypotension, hypomagnesemia in some patients, especially in patients with magnesium deficiency, glucose intolorence also has an important role in process of hyperglycemia.[23-25]

In addition to non-pharmacological and pharmacological countermeasures, the prevention of hypertension is through therapy using herbal medicines, namely using natural ingredients such as traditional medicinal plants and plants that have been clinically/preclinically tested.[7,26,27] In this study, the utilization of medicinal plants can be seen from the habits of the Chinese community in utilizing plants for hypertension by utilizing the *belalai gajah* plant (*Clinacanthus nutans* (Burm.fil.) Lindau). *Belalai gajah* plants is a member of the Acanthaceae family. This plant is popular and widespread in tropical countries such as Thailand, Malaysia, Indonesia, Africa, Brazil, and Central America.[28,29]

The *belalai gajah* plant is believed by the Chinese community as a traditional medicinal herb. The Chinese community has been known since ancient times to have used medicinal plants for treatment. It is reported that for more than 3000 years, traditional Chinese medicine has become part of the culture and tens of centuries have spread widely throughout the world, one of which is in Indonesia.[30] One of the biggest users of medicinal plants in the world is Indonesia and other Asian countries such as India and China which have been going on for thousands of years.[31,32] Scientifically *belalai gajah plants* have potential in medicine such as anticancer, antidiabetic, antibacterial, anti-inflammatory, anti-neurological inflammation, antimicrobial, antitumor and antioxidant, antibiotic, and antiapoptotic.[33-41]

Previous studies have shown that giving (*belalai gajah* plants) plants at a dose of 75 mg/kg body weight can significantly reduce blood glucose levels in diabetic rats.[42] Previously it was reported that administration of aqueous extract of *belalai gajah* plants at a dose of 150 mg/kg body weight resulted in a decrease in blood glucose levels in diabetic mice by alloxan induction.[43] In addition, it was also reported that administration of aqueous extract of *belalai gajah* plants at a dose of 75 mg/kg BW was effective in reducing blood glucose levels in diabetic rats.[44]

The assumption in society that the use of traditional medicines is safer to use when compared to modern medicines on the market, this is because natural medicinal plants do not contain substances that can be toxic to the body and traditional medicines are believed to have relatively less side effects. small. In addition, traditional medicines are easy to obtain around the neighborhood where some live, and some are deliberately planted in the yard of the house. Traditional medicines are also widely chosen because the processing is not complicated so that they can be prepared at home without the need for special equipment, and most importantly, traditional medicines are considered cheaper. The statement above is in line with previous researchers who stated that the use of medicinal plants for the treatment of hypertension is common because there are no side effects, easy to obtain, and does not require a large amount of money.[45-47] As for this study, a diuretic activity test of the *belalai gajah* plants was carried out to prove the diuretic potency of the *belalai gajah* plant in relation to its use to treat hypertension.

MATERIAL AND METHODS

Extraction stage

Belalai gajah plants are purchased at traditional markets in Pontianak. The leaves and stems of the *belalai gajah* plants that have been cleaned, weeded, and obtained a wet weight of 2,743 kg. Furthermore, the leaves and stems of the *belalai gajah* plants were dried in an open room and a sample dry weight of 486 grams was obtained. The *belalai gajah* plants were then extracted by maceration using 96% technical ethanol. The extraction process was carried out for 3 x 24 hours with replacement every 24 hours, then the macerate immersed in the sample was filtered using filter paper to obtain the first, second, and third macerate. The three macerates were combined and concentrated and from the concentration results obtained an extract weight of 53.572 grams with a yield of 11.02%.

Experimental animals

As many as 35 male white rats (*Rattus norvegicus*) Sprague Dawley strain with a body weight of 200-250 grams aged 2-2.5 months were obtained from the Laboratory of the Center for Food and Nutrition Studies, Gadjah Mada University, Yogyakarta. Prior to the experiment, all rats were acclimatized for 7 days by being given standard food and drinking ad libitum. After acclimatization, all rats were observed for their health by weighing their body weight every day at the same time. This research has been approved by the Health Research Ethics Committee at Respati University, Yogyakarta with the issuance of Ethical Clearance number 214.3/FIKES/PL/X/2021.

Testing the diuretic activity of *belalai gajah* plants

Mice were divided into 7 groups, each group consisting of 5 rats. Group I was not given the test preparation (without treatment), group II was given distilled water at a dose of 2.8 ml/200 g body weight, group III was given furosemide at a dose of 0.72 mg/200 g body weight. The dose of furosemide administration refers to Wardani (2016).[48] Group IV was given furosemide at a dose of 1.44 mg/200 g body weight. Groups V, VI, and VII were given *belalai gajah* plants extract at doses of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight. The dose of *belalai gajah* plants extract refers to Dewinta *et al*. (2020)[42] and diuretic testing following the Cumming method.[49] Mice were fasted for ± 18 hours, then their body weight was weighed. Administration of the test preparation was preceded by administering 4 ml of distilled water/200 g body weight orally (loading dose). After 30 minutes of giving the loading dose, the test preparations are given according to the group. All treatment groups were given orally to each rat using a stomach tube. After administration of the test preparation, the mice were put into individual cages (1 cage containing 1 rat).

Measurement of urine volume, urine pH, sodium levels, and potassium levels

Urine collection was carried out for 24 hours, then urine volume, and urine pH, also sodium and potassium level in rat urine in rat urine were measured. To determine the pH of urine using a pH meter. The determination of sodium and potassium levels in urine was measured using Atomic Absorption Spectrophotometry (AAS) at a wavelength of 589.0 nm for sodium and 766.5 nm for potassium.

Data analysis

This study used a completely randomize design. Urine data were analyzed using ANOVA, then data that were significantly different at the 5% level were further tested with the Duncan New Multiple Range Test using SPSS version 25.

RESULTS AND DISCUSSION

Diuretics are drugs that can increase the rate of urine production, sodium excretion, regulate the volume and composition of fluids in the body. Diuretics are used in various diseases such as congestive heart failure, nephritic syndrome, cirrhosis, kidney failure, hypertension, and toxemia,[50] and the activity and action of diuretics can be determined based on urine output.[51] The parameters used in the study of the diuretic activity of *belalai gajah* plants extracts were volume, pH, sodium levels, and potassium levels in rat urine (Table 1).

Table 1: Mean and Standard Deviation Volume, pH, Sodium Levels, and Potassium Levels Urine of Rats Without Treatment, Aquades at a dose of 2.8 ml/200 g body weight, Furosemide at a dose of 0.72 mg/200 g body weight and 1.44 mg/200 g body weight, Extract *Belalai Gajah* Plants at doses of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight.

Treatment group	Parameter			
	Urine Volume (ml)	Urine pH	Urine Sodium Level (mEq/ml)	Urine Potassium Level (mEq/ml)
Without treatment	$13.01^{a} \pm 0.07$	$7.02^{a} \pm 0.04$	$1.06^{a} \pm 0.03$	$0.5^{a} \pm 0.03$
Aquades dose of 2.8 ml/200 g body weight	$13.77^{b} \pm 0.17$	$7.11^{ab} \pm 0.02$	$1.14^{b} \pm 0.03$	$0.57^{b} \pm 0.018$
Furosemid dose of 0.72 mg/200 g body weight	$15.78^{d} \pm 0.39$	$7.21^{b} \pm 0.02$	$2.17^{f} \pm 0.09$	$0.98^{e} \pm 0.023$
Furosemid dose of 1.44 mg/200 g body weight	$18.13^{f} \pm 0.23$	$7.58^{d} \pm 0.18$	$4.01^{g} \pm 0.069$	$1.88^{f} \pm 0.04$
Belalai Gajah Plants Extract dose of 75 mg/kg body weight	$14.05^{c} \pm 0.06$	$7.15^{b} \pm 0.03$	$1.34^{c} \pm 0.08$	$0.6^{b} \pm 0.02$
Belalai Gajah Plants Extract dose of 150 mg/kg body weight	$16.78^{e} \pm 0.12$	$7.37^{c} \pm 0.03$	$1.49^{d} \pm 0.02$	$0.76^{c} \pm 0.021$
Belalai Gajah Plants Extract dose of 300 mg/kg body weight	$17.98^{f} \pm 0.09$	$7.44^{c} \pm 0.02$	$1.77^{e} \pm 0.05$	$0.87^{d} \pm 0.032$

Information:
-The number after the ± symbol indicates the standard deviation (SD) value.
-Numbers followed by different letters (a,b,c,d,e,f,g) indicate a significant difference based on Duncan's test at the 5% level.

The results of rat urine volume in administration of *belalai gajah* plants extract at a dose of 300 mg/kg body weight was 17.98 ml. The results of the urine volume from this treatment were close to the results of the urine volume produced in the group given furosemide at a dose of 1.44 mg/200 g body weight of 18.13 ml. The volume of urine in the administration of *belalai gajah* plants extract at a dose of 75 mg/kg body weight and 150 mg/kg body weight was 14.05 ml and 16.78 ml, in the administration of furosemide at a dose of 0.72 mg/200 g body weight was 15.78 ml, while the volume of urine without treatment and distilled water at a dose of 2.8 ml/200 g body weight of 13.01 ml and 13.77 ml. Based on statistical analysis, it was found that urine volume was significantly different between treatments ($p < 5\%$), except between the *belalai gajah* plants extract group at a dose of 300 mg/kg body weight and the group given furosemide at 1.44 mg/200 g body weight which was not significantly different ($p > 5\%$). Furosemide is a diuretic drug that is often used as a standard for comparison in testing diuretic activity.[18]

The average urine pH in all treatment groups was in the normal urine pH category, as stated Nurihardiyanti, Yuliet, & Ihwan (2015)[18] that the value of the degree of acidity (pH) of urine in mice can be said to be normal if it is between 7.30-8. However, statistically the rat urine pH was significantly different between treatment groups ($p<5\%$).

An increase in urine volume also results in an increase in electrolyte excretion. Diuretics are generally able to increase the excretion of urine volume, sodium, and potassium.[52] Potassium levels have an effect on blood pressure if there is an increase in sodium levels in the body, but if sodium levels in the body are normal or less then there is no effect whatsoever on blood pressure. The combination of potassium and sodium levels has a significant relationship with blood pressure when compared to only potassium or sodium levels.[53] In Table 1, the sodium level in the urine of the group given 2.8 ml/200 g of body weight was 1.14 mEq/ml, the group given 0.72 mg/200 g of body weight of furosemide and 1.44 mg/200 g of body weight were 2.17 mEq/ml and 4.01 mEq/ml, whereas in the group given *belalai gajah* plants extract doses of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight respectively 1.34 mEq/ml, 1.49 mEq/ml, and 1.77 mEq/ml. Based on statistical analysis, sodium levels in rat urine were significantly different between treatment groups ($p<5\%$).

With increasing sodium levels, there is also an increase in potassium levels in the urine. In the group given *belalai gajah* plants extract at a dose of 75 mg/kg body weight, 150 mg/kg body weight, and 300 mg/kg body weight, potassium levels in rat urine were 0.6 mEq/ml, 0.76 mEq/ml, and 0.87 mEq /ml. Potassium levels in this treatment tended to increase when compared to potassium levels in the 2.8 ml/200 g body weight aquades group, namely 0.57 mEq/ml. This happened presumably because the group experienced an increase in sodium levels in the urine, causing potassium levels in the urine to also increase. In line with the statement Tulungnen *et al*. (2016)[53] that potassium can lower blood pressure with its efficacy as a diuretic which causes an increase in sodium and fluid expenditure. The balance of sodium and potassium has an important role in maintaining blood volume. Although much of the focus is on sodium, potassium balance is also very important for blood pressure regulation and modulates the effect of sodium on blood pressure. High potassium intake can lower blood pressure by developing a balance of sodium.[54] In contrast to the diuretic effect of furosemide, the level of potassium in the urine in the group receiving the *belalai gajah* plants extract was not as high as the potassium level in the urine in the group receiving furosemide at doses of 0.72 mg/g body weight and 1.44 mg/g body weight, namely 0.98 mEq/ml and 1.88 mEq/ml. In measuring potassium levels, the group without treatment showed the lowest compared to the other treatments, namely 0.50 mEq/ml. Statistically, the levels of potassium in the urine were significantly different between treatment groups ($p<5\%$). Furthermore, from Table 1. it is known that *belalai gajah* plants extracts have diuretic properties, and their diuretic properties are different from distilled water and furosemide. Apart from increasing urine volume, *belalai gajah* plants extracts also increase sodium and potassium levels in urine, but tend to be sparing of potassium. It is assumed that the *belalai gajah* plants extract has a potassium-sparing diuretic mechanism.

Potassium-sparing diuretics are most often used to correct potassium deficiency in hypertensive patients or to treat primary aldoteronism.[55] The mechanism of action of potassium-sparing diuretics acts in the distal convoluted tubule and in the collecting ducts by inhibiting sodium/potassium exchange or blocking apical sodium channels (amiloride and triamterene) and antagonizing mineralocorticoid receptors (eplerenone and spironolactone). Eplerenone and spironolactone are competitive antagonists of the effects of aldosterone on the distal tubule. All are weak diuretics but are particularly effective antihypertensive agents in low-renin (salt-dependent) hypertension.[13,56-59]

CONCLUSION

Belalai gajah plant extract has diuretic properties, and its mechanism of action is as a potassium-sparing diuretic.

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