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ACTIVITY TEST OF SIAM LABU (*Sechium edule* (Jacq.) Swartz) LEAF EXTRACT ON REDUCTION OF DARAGE URATE ACID TARGETS OF WHITE RATS (*Rattus novergicus*)

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ABSTRACT

Uric acid is a substance produced from the breakdown of purines or waste products in the body, as a result of purine catabolism aided by the enzymes cguanase and xanthine oxidase. One of the green plants used as traditional medicine is siam labu (*Sechium edule*). This plant is a vegetable plant belonging to the Curcubatiacae family that grows in the highlands. The purpose of this study was to test the anti-gout activity of chayote leaves in male rats. The method used in this study started from preparing simplisia, preparing siam labu leaf extract, inducing mice with Ca-oxanate at a dose of 250 mg/kgBW and administering siam labu leaf extract at a dose of 250 mg/kgBW, 500 mg/kgBW. and 750 mg/kgBW was administered orally with intermittent observation periods of 1 hour for 6 hours. Results obtained in rats given 750 mg/kgBW of extract showed the lowest reduction of 3.88 ± 0.3 mg/dl. One-way ANOVA results obtained a significant value p=0.00 (p<0.05), which can be concluded that there are differences in each treatment method in experimental animals. Tukey test results can be seen at 6 hours, it can be concluded that EDLS 750 mg/kg body weight with allopurinol is not significantly different.

Keywords: *Uric Acid, Extract Siam Labu, Rats, Allopurinol*

Introduction

Uric acid is a substance produced from the breakdown of purines or waste products in the body, as a result of purine catabolism aided by the enzymes cguanase and xanthine oxidase. High uric acid levels will lead to an increase in needle-shaped uric acid crystals, especially in the joints, which will cause joint pain. This condition is called gout or pirai arthritis (Ningtiyas and Ramadhian, 2016). Using synthetic chemical medications in people with gout can cause side effects, including pain when urinating, bleeding urine, dark urine, or even decreased urine output. Long-term use of gout medications can cause kidney problems (Tayeb et al., 2016).

Hyperuricemia is a condition in which uric acid levels in the blood increase above normal levels, more than 7 mg/dl (>420). Hyperuricemia may result from increased uric acid metabolism (overproduction),

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decreased urinary excretion of uric acid (underexcretion), or a combination of both. Plasma uric acid is an inflammatory agent. Uric acid stimulates macrophages to produce inflammatory cytokines, specifically interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin 8 (IL-8), and tumor necrosis factor-α (TNF-α). 17 TNF-α and IL-1 released by peripheral blood platelets can activate the expression of E-selectin in vascular endothelial cells, intercellular adhesion molecule 1 (ICAM-1), and ICAM-first. This will stimulate leukocyte withdrawal to the monosodium urate area and increase the inflammatory response (Putra, 2006).

One of the green plants used as traditional medicine is siam labu (*Sechium edule*). This plant is a vegetable plant belonging to the Curcubatiacae family that grows in the highlands. According to experience, Siam labu leaves (*Sechium edule*) are used by the community to treat kidney stones, arteriosclerosis and high blood pressure. While the fruit is often used to reduce urinary retention. Siam labu has diuretic effects, treats mouth ulcers, internal heat, reduces fever in children and is well used by people with gout (Sultani, 2014).

According to experience, chayote leaves (*Sechium edule*) are used by humans to treat kidney stones, arteriosclerosis and high blood pressure. While the fruit is often used to reduce urinary retention. Chayote has diuretic effects, treats mouth ulcers, internal heat, reduces fever in children and is well used by people with gout (Priantono, 2005).

According to Arifurahman (2017), chayote leaves contain alkaloids, saponins, steroids, tannins and flavonoids, steroids, triterpenoids and glycosides. According to research by Rizki et al. (2014), antioxidant activity testing was performed with chayote leaf extract in ethanol using the DPPH method. Research results show that the ethanolic extract of chayote leaves has very strong antioxidant activity with an IC50 value of 3.8 µg/ml.

Based on the above background, the researchers wanted to conduct a study testing the anti-reducing activity of uric acid levels in white male rat.

Materials and Methods

Research Materials

Ingredients used in the study were Siam Labu leaf extract, CMC, potassium oxanate and allupurinol.

Research Procedure

This study began with the production of simplex and testing the properties of simplex in the form of determining water content, water-soluble water content, ethanol-soluble water content, and total ash content. Additionally, phytochemical screening of the obtained simplification was performed.

Extract Preparation Procedure

Put 500 g of simplisia powder in a sealed container, then pour in 75 parts of 96% ethanol and soak for 5 days, stirring occasionally. After 5 days, the solution mixture was separated by filtration, separating the filtrate and the residue (maserat I). The residue was soaked again with 25 parts of 96% ethanol for 2 days, then filtered (maserat II), maserat I and maserat II combined. Then, the clear liquid was removed and concentrated into a rotary evaporator at 500°C until a concentrated extract was obtained (Ministry of Health of the Republic of Indonesia, 1989).

Preparation of Potassium Oxanate

The preparation of potassium oxanate solution is carried out as follows: Weigh 250 mg of potassium oxanate into a 10 ml volumetric flask, add 0.9% NaCl solution to the limit mark.

Pharmacological Testing

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Selection and Preparation of Test Animals

The test animals used in this study were 3 to 4 months old and weighed 150 to 200 g. Before use, animals were acclimatized for 14 days by providing them with adequate nutrition and a clean environment.

This experiment was performed with 5 treatments and divided into 5 groups, to determine the number of experimental animals in each group and to obtain valid data, replications were performed according to the formula of Federer (1997): (n-1) (t-1) ≥15, where t represents the number of treatments and n indicates the minimum number of repetitions of each treatment (Sudjana, 1992).

Treatment of Test Animals

The test animals used in this study were white male mice weighing an average of 150 to 200 grams and were 3 to 4 months old. Test animals were first acclimated to the study environment for 1 day and fed for ±18 h before the start of the study, while still drinking water. The animals were divided into 5 groups, each group consisting of 5 mice, then each mouse in the group was weighed and marked on the tail. Each group measured fasting uric acid levels by dropping blood from the mouse tail vein onto the test strip, waiting a few seconds until the blood automatically distributed evenly throughout the reaction area. Within 6 seconds, the mouse's blood uric acid concentration appeared on the device screen, after which the mouse was injected with a dose of 250 mg/kg BB potassium oxanate intraperitoneally (i.p). One hour later, uric acid levels are measured. . After measuring uric acid levels, each mouse was treated as follows:

- Group I: Negative control (-), given 0.5% CMC
- Group II: Positive control (+), given allopurinol 100 mg / kg BW
- Group III: Given a dose of chayote leaf extract 250 mg / kg BW
- Group IV: Given chayote leaf extract at a dose of 500 mg / kg BB
- Group V: Given a dose of chayote leaf extract 750 mg / kg BB

One hour later, the male mice's uric acid levels were measured and again after 2 hours, 3 hours, 4 hours, 5 hours, and 6 hours in the same way.

Data Analysis

After obtaining data to show the effect of using the test material in reducing uric acid levels in the blood of mice, the data will be statistically analyzed using One-Way Annova and Post huc tuckey with a 95% confidence level. This statistical analysis used the SPSS version 20.0 program.

Results and Discussion

Characteristics of Siam Labu Leaf Simplisia

Characterization of Simplisia includes determination of water content, total ash content, acid soluble ash content, water soluble juice content, ethanol soluble juice content, performed with The purpose is to ensure consistency in the quality of Simplisia to meet the requirements of the Simplisia Standard. The results of investigating the characteristics of Siam Labu simplisia leaf powder are presented in **Table 1**.

Table 1 Characterization Results of Siam Labu Leaf Simplisia Powder

Parameters	Inspection Result (%)	MMI Requirement (1989)
Moisture content	8	<10%
Water soluble juice content	21	8-30%

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Ethanol soluble juice content	14	5-26%
Total ash content	16,66	7-17%
Acid soluble ash content	23,3	1-10%

Determining the moisture content of simplisia is important to set a maximum limit on the water content in simplisia because large amounts of water can become a suitable environment for bacterial and fungal growth that can damage the compounds. contained in simplisia (Ministry of Health) of the Republic of Indonesia, 2000). Simplified water content requirements according to current standard parameters do not exceed 10%. Test results of water content of simplisia leaves at 8% show that simplisia meets the standard water content of syrup.

The determination of water and water soluble content in ethanol was carried out to give a first description of the number of compounds that can be extracted with water and ethanol solvents from a simple one (Ministry of Health of the Republic of Indonesia, 2000). Test results show that the water-soluble water content of chayote leaves has a value of 27%, while the water-soluble water content of ethanol is 16%. This proves that the number of polar compounds that can be dissolved in water is greater than the number of less polar compounds (semi-polar and non-polar) that can be dissolved in ethanol. This test result still meets the requirements.

Determination of total ash content is carried out with the aim of providing insight into the internal and external mineral content obtained from the initial process through to simple formation. The total ash content is related to organic and inorganic mineral compounds obtained internally and externally. At the same time, the acid-insoluble ash content is intended to determine the amount of ash obtained from external factors, originating from impurities from sand or silicate soil (RI Ministry of Health, 2000). According to test results, the total ash content is 16.6% and the acid-insoluble ash content is 23.3%. According to MMI (1989), the acid-insoluble ash content does not meet the requirements. This is due to the poor cleaning process at the washing stage of fresh ingredients.

Phytochemical Screening of Siam Labu Leaf Extracts

Phytochemical testing of Siam Labu leaf extract was performed to collect information on the group of secondary metabolites present in Siam Labu leaf extract. Screening results can be alkaloids, flavonoids, saponins, tannins, steroids/triterpenoids. Phytochemical screening results of Siam Labu leaf extract are shown in **Table 2.**

Table 2. Phytochemical Screening Results of Siam Labu Leaf Extracts

Secondary Metabolits	Results
Alkaloids	+
Flavonids	+
Saponins	+
Tannins	+
Steroids/triterpenoids	+

Description: (+) = Contains a class of secondary metabolite compounds
(-) = Does not contain secondary metabolite compounds

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The phytochemical screening results obtained are consistent with researcher Erawati (2015), who said the phytochemical screening test of chayote leaf extract showed the presence of alkaloid compounds, flavonoids , saponins, tannins, steroids/triterpenoids.

Measurement of Uric Acid Levels of Each Experiment in Experimental Animals

An increase in uric acid concentration of each group could be observed after induction treatment with potassium oxanate at a dose of 250 mg/kg body weight. Subsequently, a decrease in uric acid levels was observed 6 (six) hours after treatment in the form of CMC 0.5%, allupurinol 100 mg/kg body weight, EDLS 250 mg/kgBB, 500 mg/kgBB, 750 mg/kgBB. . The decrease in uric acid levels can be seen in **Table 3.**

Table 3 Mean Uric Acid Level ± SD of Each Treatment in Experimental Animals

Groups	Mean Fasting Uric Acid ± SD (mg/dl)	Mean Uric Acid Level After Ca-Oksanat Induction	Rata-rata kadar asam urat setelah pemberian perlakuan ± SD (mg/dl)					
			1	2	3	4	5	6
K1	3,74±0,15	8,06±0,24	7,92±0,2	7,76±0,2	7,6±0,2	7,46±0,3	7,38±0,2	7,24±0,3
K2	3,3±0,15	7,58±0,46	6,74±0,6	6,06±0,5	5,38±0,5	4,82±0,8	4,02±0,5	3,46±0,2
K3	3,2±0,35	7,88±0,46	7,58±0,4	6,94±0,3	6,16±0,5	5,52±0,3	4,9±0,5	4,12±0,4
K4	3,8±0,41	7,96±0,30	7,44±0,3	6,88±0,4	5,88±0,6	5,32±0,4	4,7±0,2	4,08±0,2
K5	3,66±0,45	7,86±0,24	7,16±0,2	6,48±0,3	5,88±0,2	53±0,3	4,5±0,3	3,88±0,3

Description:
K1 = CMC 0.5%
K2 = Allupurinol 100 mg/kg BW
K3 = EDLS 250 mg/kgBW
K4 = EDLS 500 mg/kgBW
K5 = EDLS 750 mg/kgBW

Based on table 3 above, it can be seen that there is a difference in the degree of reduction in blood uric acid concentration of male mice in the positive group, the group tested with the extract dose of 250 mg/kgBW, the dose of 500 mg/kgBW and 750 mg. . /kgBW while negative group or CMC administration had no such effect in reducing uric acid levels in male mice.

From the table it can be seen that in this study, a decrease in uric acid levels occurred in the positive control group, followed by 3 dose change groups. Specifically, the 750 mg/kgBW dose group changed, then the 500 mg/kgBW dose group and the 250 mg/kgBW dose group. This suggests that chayote leaf extract may provide activity in reducing uric acid levels and that a dose of 750 mg/kgBW of chayote extract is the most effective dose for reducing uric acid levels.

Based on table 3 above, it can be concluded that the significant value is less than 0.05 ($p < 0.05$). It is said that there are significant differences between each treatment in terms of reducing uric acid levels. We then continued with the Post

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Hock Tukey test, which aimed to determine which groups had a significant difference in reducing uric acid levels. The results of Post Hock Tukey can be seen in appendix 19, it was found that in the first hour there was no significant difference in each group. Then, between hour 2 and hour 6, there were significant differences between the negative groups with EDLS doses of 250 mg/kg body weight, 500 mg/kg body weight, 750 mg/kg body weight and allopurinol. This means that EDLS and allopurinol were more effective in reducing uric acid levels in male rats than the control (-) CMC 0.5%.

Conclusions

Based on the study on the activity of pumpkin leaf extract, it can be concluded that Siam Labu leaf extract shows the presence of secondary metabolites, which are alkaloid compounds, flavonoid tannins, saponins and steroids/triterpenoids. The dose variations used to reduce uric acid levels in male rats were 250 mg/kg body weight, 500 mg/kg body weight, and 750 mg/kg body weight. The dose of 750 mg/kgBW is most effective in reducing uric acid levels. There were significant differences in each group in that EDLS and allopurinol reduced uric acid levels better than the negative control group.

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