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Evaluation of the Antihyperuricemia Activity of Bajakah Tampala Stem Ethanol Extract (*Spatholobus littoralis* Hassk.) in Male White Mice (*Mus musculus*)

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Abstract

Hyperuricemia is elevated blood uric acid. Blood uric acid can harm health. Allopurinol can lower uric acid, but it has harmful side effects. The community has treated various diseases with Bajakah stems. This study examined Bajakah Tampala stem ethanol extract secondary metabolites and antihyperuricemia activity. This research identified the bajakah tampala stem plant (Spatholobus littoralis Hassk.), manufactured simplicia, characterized simplicia, phytochemically screened, prepared the ethanol extract, and tested its antihyperuricemia activity against male white mice (Mus musculus). The simplicia and Bajakah tampala stem ethanol extract contained flavonoids, tannins, steroids/triterpenoids, alkaloids, and saponins. At 400 mg/kgBB (3.88 mg/dl), the bajakah tampala stem ethanol extract reduces uric acid at the 6th hour, similar to allopurinol at 10 mg/kgBB (3.46 mg/dl).

Keywords: *Bajakah tampala stem,Spatholobus littoralis, Hyperuricemia, Allopurinol*

Abstrak

Hiperurisemia adalah peningkatan asam urat darah. Asam urat darah dapat membahayakan kesehatan. Allopurinol dapat menurunkan asam urat, namun memiliki efek samping yang berbahaya. Masyarakat telah mengobati berbagai penyakit dengan batang Bajakah. Penelitian ini menguji metabolit sekunder ekstrak etanol batang Bajakah Tampala dan aktivitas antihiperurisemia. Penelitian ini mengidentifikasi tanaman batang bajakah tampala (Spatholobus littoralis Hassk.), pembuatan simplisia, karakterisasi simplisia, skrining fitokimia, preparat ekstrak etanol, dan uji aktivitas antihiperurisemia terhadap mencit putih jantan (Mus musculus). Simplisia dan ekstrak etanol batang bajakah tampala mengandung flavonoid, tanin, steroid/triterpenoid, alkaloid, dan saponin. Pada 400 mg/kgBB (3,88 mg/dl), ekstrak etanol batang bajakah tampala menurunkan asam urat pada jam ke-6, mirip dengan allopurinol pada 10 mg/kgBB (3,46 mg/dl).

Kata Kunci*: Batang bajakah tampala, Spatholobus littoralis, Hiperurisemia, Allopurinol*

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INTRODUCTION

The prevalence of hyperuricemia has increased worldwide, both in developed and developing countries. Based on data from the Global Burden of Diseases (GBD), it shows that the prevalence of hyperuricemia in Indonesia is 18%. Hyperuricemia data were also obtained from Tomohon City and Denpasar, where the prevalence

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reached 25% and 18.2%, respectively. Whereas in Bandungan (Central Java), the figures were 24.3% for men and 11.7% for women, with a total prevalence of both sexes of 17.6%[1].

Hyperuricemia is a condition where uric acid levels in the blood are greater than the normal value, which in men is said to be hyperuricemia if the uric acid levels are above 7 mg/dl and in women above 6 mg/dl. Mice are said to have hyperuricemia when their uric acid levels are 1.7–4.0 mg/dl[2].

Medications used to lower blood uric acid levels can be used by either reducing uric acid production or increasing uric acid excretion by the kidneys. Allopurinol is an example of a drug that works to inhibit the formation of uric acid through inhibition of the activity of the enzyme xanthine oxidase, and probenisid is an example of a uricosuric drug that can increase uric acid excretion by inhibiting its reabsorption in the kidney tubules[3].

One of the plants that has the potential to be used as a traditional anti-hyperuricemia medicine is bajakah tampala (Spatholobus littoralis Hassk.). Compounds that have potential as antihyperuricemia agents are flavonoids, tannins, and saponins. Flavonoid group compounds work by inhibiting xanthine oxidase so as to reduce excessive uric acid production; tannin compounds are known to bind free radicals during the conversion of purines to uric acid; and saponin compounds work by reducing the activity of the xanthine oxidase enzyme in serum[4]. Aside from being antihyperuricemia, flavonoids also function as anti-inflammatories by inhibiting cyclooxygenase and lipooxygenase enzymes so that they can reduce pain resulting from hyperuricemia[5].

According to previous research, the ethanol extract of the Bajakah tampala stem has secondary metabolite compounds like phenolics, flavonoids, tannins, and saponins and helps male rats heal wounds[6]. The Bajakah Tampala stem ethanol extract is antibacterial[6] and antioxidant[7]. The ethanol extract of Bajakah tampala stem was tested for antihyperuricemia (*Spatholobus littoralis* Hassk).

METHODOLOGY

Identification of the bajakah tampala stem plant (*Spatholobus littoralis* Hassk.), collection of the bajakah tampala stem plant, production of simplicia, characterization of simplicia, phytochemical screening, preparation of the ethanol extract of the bajakah tampala stem, and antihyperuricemia activity test of the

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ethanol extract of the bajakah tampala stem (*Spatholobus littoralis* Hass (Mus musculus).

Sample Processing

The samples used were tampala pirate stems taken from Central Kalimantan. The stems of the Bajakah Tampala that have been collected are washed thoroughly with running water, then drained and spread on parchment paper. The ingredients are then chopped, weighed, and dried in a drying cupboard at 40°–50°C until dry; when crushed, they are brittle. The dried simplicia was then powdered using a blender[8]. The simplicia powder is stored in plastic to prevent moisture and other impurities before being extracted.

Preparation of Bajakah Tampala (Spatholobus littoralis Hassk.) Stem Ethanol Extract

The ethanol extract of the stem of Bajakah tampala (*Spatholobus littoralis* Hassk.) was made by percolation using 96% ethanol solvent by means of 500 g of simplicia powder moistened with 250 ml of solvent, closed, and left for 3 hours, then put into a percolator. Pour enough of the 96% ethanol solvent solution until all the simplicia is submerged and there is a layer of solvent above it[9]. The mouth of the percolator tube is covered with aluminum foil and left for 24 hours, then the faucet is opened and the extract droplets are allowed to flow at a rate of 1 ml per minute, and the percolate is collected. Add the filter solution repeatedly so that there is always a layer on top, so that you get 4 liters (80 parts). The percolation was stopped when the last 500 g of percolate had been evaporated without leaving any residue, and then sufficient distiller solution was added to obtain 5 liters (100 parts)[10]. The extract was evaporated using a rotary evaporator until a thick extract was obtained[11].

Preparation of 0.5% Na Carboxymethyl Cellulose (Na CMC) Suspension

As much as 0.5 g of CMC Na was put into a mortar containing 10 ml of hot distilled water and allowed to stand for 15 minutes until a transparent mass was obtained, then crushed until homogeneous. Then it was diluted with distilled water and put into a 100-ml volumetric flask. The volume is turned all the way up[12].

Preparation of Bajakah Tampala Stem Ethanol Extract Suspension (Spatholobus littoralis Hassk.)

The dose of the ethanol extract of the Bajakah tampala stem was determined based on the orientation of the dose in experimental animals. The doses of the ethanol extract of

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Bajakah stems given to experimental animals were 200, 300, and 400 mg/kgBB. The ethanol extract of the bajakah stem (EEBBT) was weighed at 200, 300, and 400 mg, respectively, and put into a mortar containing a small amount of 0.5% Na CMC suspension, homogenized, and then added to 10 ml of the 0.5% Na CMC suspension.

Preparation of 1% Allopurinol Suspension

Allopurinol 100 mg, as much as 1 tablet, was crushed into a mortar, then 0.5% Na CMC suspension was added little by little while grinding until homogeneous, and the volume was made up to 100 ml with 0.5% Na CMC.

Preparation of Potassium Oxonate Solution

The preparation of a potassium oxonate solution is carried out in the following way: 250 mg of potassium oxonate are weighed, then put into a 10-ml volumetric flask, and 0.9% NaCl solution is added to the mixture[12].

Uric Acid Lowering Effect Testing

This study used healthy male white mice (Mus musculus) weighing 20–30 g. The study was conducted with five treatment groups. The total number of animals used from each treatment group was determined based on the Federer formula[13].

The study began with mice being fasted for 18 hours (not given food but given water). Then each mouse was weighed and marked. Then the fasting uric acid level was measured by dripping blood from the tail vein of the mice onto the test strip and waiting a few seconds until the blood was evenly distributed in the reaction zone automatically. Within 20 seconds, the level of uric acid in the blood of the mice will appear on the screen of the tool. The mice were then given an intraperitoneal (i.p.) injection of 0.2 mL potassium oxonate. Mice were randomly divided into 5 groups, and each group's uric acid levels were measured after one hour of injections of potassium oxonate. After measuring uric acid levels, each rat was treated as follows:

1. Group 1: As a negative control, give CMC Na 0.5% orally.
2. Group 2: Allopurinol 1% was given orally as a positive control.
3. Group 3: Given EEBBT at 200 mg/kgBB, orally
4. Group 4: Given EEBBT at 300 mg/kgBB, orally
5. Group 5: Given EEBBT 400 mg/kgBB, orally

Blood uric acid levels were measured again one hour after the test material was administered, then again after two hours, four hours, six

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hours, and until the mice's uric acid levels returned to normal[14].

Data analysis

Data analysis from this study was carried out by calculating the average decrease in uric acid levels for each group using the normality and homogeneity method, one-way ANOVA (analysis of variance), followed by the Tukey test to see significant differences between treatment groups. This statistical analysis uses the SPSS (Statistical Product and Service Solution) program.

RESULT AND DISCUSSION

Plant Identification

In a study involving plants, the initial step is determination. This plant identification aims to ascertain and confirm the correct identity of the plants used and to prevent sampling errors. Plant identification performed at the Medanense Herbarium (MEDA) of the Biology Research Center, Faculty of Mathematics and Natural Sciences, University of North Sumatra revealed that the plant used in this study was the stem of the tampala bajakah (*Spatholobus littoralis* Hassk.). Local name: (Bajakah Tampala) In Figure 1, the tampa steel rod can be seen.

Figure 1. Tampala Bajakah Stem

Simplicia Characterization of Bajakah Tampala (Spatholobus littoralis Hassk.) Stems

The results of the characterization of the simplicia powder from the Bajakah Tampala stem can be seen in Table 1.

Table 1. Powder Characterization Results of Bajakah Tampala Stem Simplicia

No	Parameter	Check up result (%)	MMI terms (%)
1.	Water content	7.3%	< 10%
2.	Water soluble essence content	13.3%	> 9%
3.	Ethanol soluble essence content	16%	> 7%
4.	Total ash content	3.17%	< 10%
5.	Acid insoluble ash content	0.5%	< 1%

According to Materia Medica Indonesia, the results of the characterization tests for water content, water-soluble essence

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content, ethanol-soluble extract content, total ash content, and acid-insoluble ash content are satisfactory.

Phytochemical Screening

A phytochemical screening was conducted to determine the class of secondary metabolites present in the stem of the Bajakah Tampala plant. Table 2 displays the screening results for simplicia powder and the ethanol extract of the Bajakah Tampala stem.

Table 2. Results of Phytochemical Screening of Bajakah Tampala Stems

No	Secondary Metabolites	Powder Results	Extract Results
1.	Alkaloids	+	+
2.	Flavonoids	+	+
3.	Saponins	+	+
4.	Tanins	+	+
5.	Steroids/Triterpenoids	+	+

Information
(+) indicates that secondary metabolites are present.
(-) Negative: Does not contain secondary metabolite

The ethanol extract of the Bajakah tampala stem contains secondary metabolites of alkaloids, flavonoids, saponins, tannins, steroids, and triterpenoids. The presence of flavonoids contained in this plant is very supportive as an antihyperuricemia drug. Flavonoids act as xanthine oxidase inhibitors because flavonoids are reducing agents, so they can inhibit the action of the xanthine oxidase enzyme to convert xanthine compounds into uric acid.

Measurement of Uric Acid Levels in the Ethanol Extract of Bajakah Tampala Stems

This study used experimental animals, namely mice, because mice have a digestive system absorption process and a metabolic system for testing drugs that are relatively similar to the human digestive system. The selection of male mice as test animals is because male mice have greater hormonal stability compared to female mice, because female mice experience estrus cycles during pregnancy and lactation, which will affect the psychological condition of the test animals. Male mice do not have the hormone estrogen, even though there is a very small amount. The hormone estrogen is useful for increasing uric acid excretion through urine. Increased levels of uric acid in each group can be observed after the

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induction process using potassium oxanate. Then the decrease in uric acid levels was observed for six (six) hours after being given treatment in the form of 0.5% Na CMC, allopurinol, EEBBT 200 mg/kgBB, EEBBT 300 mg/kgBB, and EEBBT 400 mg/kgBB. The decrease in uric acid levels can be seen in Figure 2.

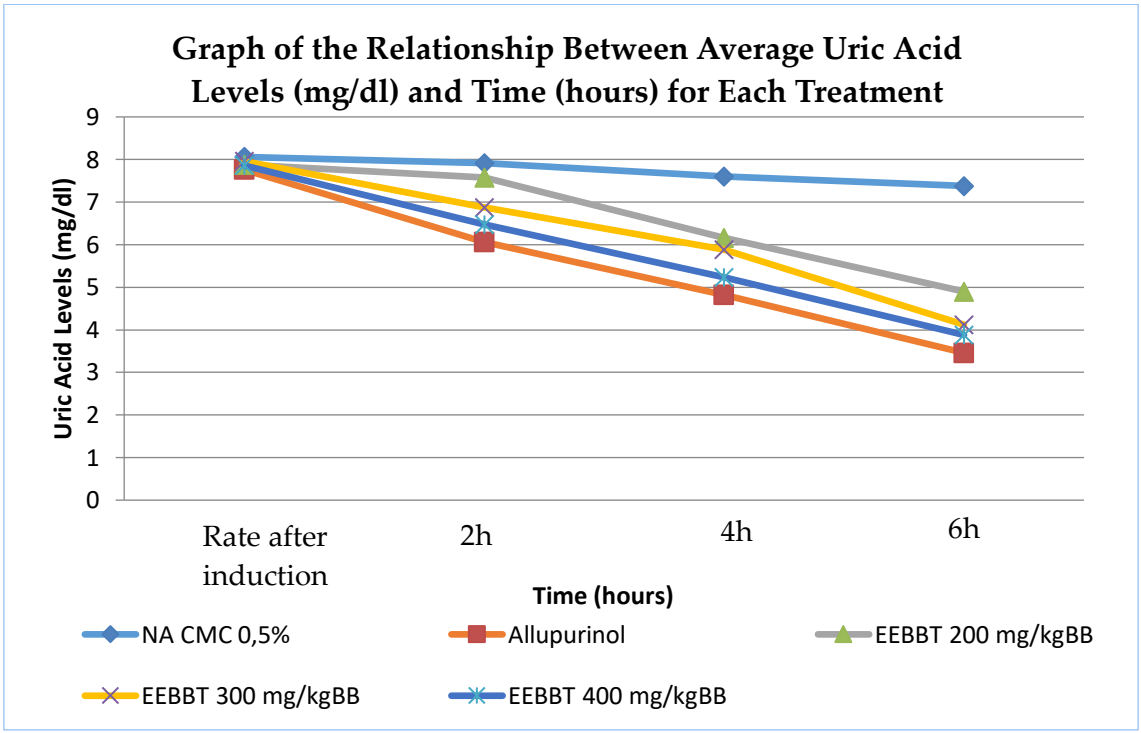

Figure 2. Graph of the Relationship Between Average Uric Acid Levels (mg/dl) and Time (Hours) for Each Treatment

Based on Figure 2 above, the EEBBT uric acid level test of 200 mg/kgBB decreased uric acid levels at the 4th hour and continued to decrease uric acid levels until the 6th hour. where EEBBT at 300 mg/kgBB and 400 mg/kgBB decreased uric acid levels at the 2nd hour. At the sixth hour, EEBBT of 400 mg/kgBB was nearly as effective as allopurinol uric acid reduction. Based on the graph above, to find out the differences in uric acid levels in mice obtained from various different treatments, whether significant or not, it is necessary to proceed with the one-way ANOVA test and the Tukey test.

In the one-way ANOVA test, if the significant value shows (0.05), it means that there is a significant difference in ability, and if the value shows (0.05), it means that there is no significant difference in ability[15].

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In this study, measurements of decreased uric acid levels in mice had a significant value of 0.05, indicating a significant difference. The Tukey test was continued to see if there were differences in the data on the decrease in uric acid levels in the test animals from before treatment to after treatment between the 5 different treatment groups. Whereas data from normal levels and levels after induction show no significant change, allopurinol is already significant at 2 hours EEBBT at 400 mg/kgBB. At 4 hours EEBBT, 400 and 300 mg/kgBB were significant with allopurinol. while the EEBBT dose of 200 mg/kg BB was not significant until 6 hours.

The effectiveness of reducing uric acid from the Bajakah Tampala stem is strongly supported by the presence of secondary metabolites contained therein. The flavonoid group is one of the secondary metabolite compounds found in the stem of Bajakah tampala as a result of phytochemical screening[16]. Flavonoids are one of the compounds that are most likely to act as xanthine oxidase inhibitors because flavonoids are reducing agents, so they can inhibit the action of the xanthine oxidase enzyme to convert xanthine compounds into uric acid[17].

Overall, it can be concluded that the ethanol extract of the Bajakah Tampala stem has effectiveness for reducing uric acid in male white mice induced with potassium oxonate; the best dose is 400 mg/kgBB, which is not significantly different from allopurinol 10 mg/kgBB in the 6th hour after administration of the test substance.

CONCLUSION

The ethanol extract of the Bajakah tampala stem contains secondary metabolites of alkaloids, flavonoids, saponins, tannins, steroids, and triterpenoids. The ethanol extract of bajakah tampala stems has an antihyperuricemia effect in mice at the three doses used: 200, 300, and 400 mg/kgBB. EEBBT 300 and 400 mg/kgBB have comparable effectiveness with allopurinol 10 mg/kgBB; the statistical test results for EEBBT 300 and 400 mg/kgBB are not significantly different ($p > 0.05$) with allopurinol 10 mg/kgBB at 4 hours and 6 hours. The 200 mg/kgBB dose was significantly different from the 10 mg/kgBB allopurinol dose (p 0.05). The most effective dose of the ethanol extract of Bajakah Tampala as an antihyperuricemic is 400 mg/kgBB.

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