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PERBANDINGAN AKTIVITAS ANTI-HIPERURISEMIA EKSTRAK ETANOL SELEDRI *(APIUM GRAVEOLENS L.)* DAN DAUN SALAM (*SYZYGIUM POLYANTHUM*) PADA MENCIT YANG DIINDUKSI KAFEIN

ANTIHYPERURICEMIC ACTIVITY OF ETHANOL EXTRACTS FROM CELERY PLANTS (APIUM GRAVEOLENS L.) AND BAY LEAVES (SYZYGIUM POLYANTHUM) IN CAFFEINE-INDUCED HYPERURICEMIC MICE MODEL

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Abstract

Celery plants (*Apium Graveolens L*) and bay leaves (*Syzygium polyanthum*) have been used as alternative medicine to treat Hyperuricemia. This study aimed to determine the effectiveness of administration of extracts from celery plants and bay leafs to decrease uric acid levels in blood. This research used a post-test control group only design. A total of 24 male mice (randomly divided into 4 groups; P0, P1, P2 and P3). P0 was the control group (induced with caffeine at a dose of 0.5 mg/kgBW). P1 was induced with caffeine 0.5 mg/kgBW+celery extract 35 mg/kgBW, P2 was induced by caffeine 0.5 mg/kgBW+bay leaf extract 35 mg/kgBW and P3 was induced by caffeine + a combination of celery plant extract and bay leaves 35mg/kgBW. Uric acid levels were measured using an easy touch GCU meter device. The results showed that average of uric acid level for P0, P1, P2 and P3 were 7.1mg/dl; 4.9 mg/dl; 4 mg/dl; and 5.2 mg/dl, respectively. The most significant antihyperuricemia activity was demonstrated by administering 35 mg/kgBW of bay leaf extract. The One Way ANOVA analysis described that the administration of extract ethanol of celery, bay leaves and combination generated significant effects in lowering the levels of uric acid (p-value <0.05). Based on post hoc LSD analysis, it was found that groups of P1, P2 and P3 have statistically differences in their means to P0 as well as groups of P2 to P3. However, the antihyperuricemic activity showed insignificant difference between P1- P3 and P1-P2.

keywords: bay leaf extract, celery extract, caffeine-induced mice, ethanol extract, dan mouse-model

INTRODUCTION

Indonesia's biodiversity is a significant asset for the progression of scientific research in the traditional medicine sector. Around 30,000 different types of flora are found in Indonesia with 940 types of therapeutic characteristics which have been used as traditional medicines (Darussalam & Kartika Rukmi, 2019). The use of medicinal plants as alternative treatments is generally considered safer than the use of modern medicine due its lack of side effects (Astuti, 2018). Hyperuricemia is a prevalent ailment among individuals in Indonesia across all socioeconomic strata. This disease is the third common diseases found in Indonesia after rematoid arthritis (Pertiwi, 2016).

Recently, common medication to treat hyperurichemia is to consume chemical drugs such as allopurinol. Allopurinol is widely known for its activity as antihyperurichemia, however long-term consumption potentially causes side effects such as allergic reactions/rashes and vasculitis (Emad, Dalbeth, Weinman, Chalder, & Petrie, 2022). Consequently, alternative therapy is required in order to lower the level of uric acid and lessen the negative effects of contemporary medication. Celery is one of antioxidant sources due it its high level of flavonoid and this plant has been used by Indonesian to treat hyperurichemia for decades (N. Wahyuni & Awaludin, 2023)

Bay leaves are also known for their effectiveness in lowering uric acid level. The antihyperuricemic properties of bay leaf extract have been demonstrated by pharmacological studies. According to earlier studies, male mice given 250 mg/KgBW of caffeine were able to lower their uric acid levels when given 200 mg/KgBW of bay leaf extract. Furthermore, studies conducted by (Pratiwi, 2021) revealed that male mice treated with 37.8 mg/kgBW of caffeine showed a significant reduction in blood uric acid levels when exposed to 400 mg/kgBW of bay leaf ethanol extract.

Several studies have illustrated antihyperuricemic activity of celery extract and bay leaves extract. However, there was lack of study examining the comparison of antihyperuricemic's effectiveness between celery and bay leaves extracts in decreasing the level of uric acid in blood.

This research aimed to investigate the comparison of the antihyperuricemic activity from ethanol extract of celery and bay leaves. This research was in-vivo study that measured the effectiveness of antihyperuricemic properties from those two plants in caffeine-induced hyperuricemic mice model.

MATERIALS AND METHODS

Chemical and Reagents

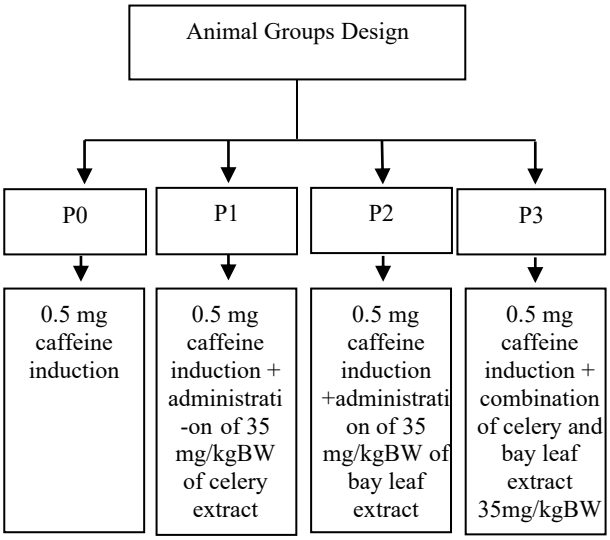
Tools in study included easy touch GCU, Erlenmeyer flask, blender, scissors, measuring cylinder, rotary evaporator, water bath, strain, spatula, analytical balance, silica TLC plate, sonde (feeding tube), ethanol 96%, purified caffeine, aquadest, and ad libitum diet

Plant materials

Apium graveolens L. plants and *Syzygium polyanthum* leaves were collected and identified. The simplisia were dried using air drying methods. The dried samples were grounded with a blender until a coarse powder was obtained. Each 200 g of dried celery plants and bay leaves were extracted using ethanol 96% and a rotary vacuum evaporator was performed to obtain crude ethanol extracts. After evaporated, the extract was re-evaporated using water-bath until the viscous or solid residue was obtained.

Animal Design

This research is a laboratory experimental research using Post-Test Control Group Only Design (Sani K, 2016). Twenty-four of male Mus Musculus L (Bal C), aged of 2-3 months (20 – 30 gr) were supplied by pharmacological laboratory of Universitas Sumatera Barat. Hyperuricemia in the mice was induced by caffeine, administered caffeine for seven consecutive days (0,5 mg/100 ml) as previously described (Mahmudah, Yusuf, & Nur, 2023). The mice were divided into 4 groups randomly (n= 6 each); the model control group – caffeine-induced mice model, Po, model mice + celery extract group (35 mg/kg), P1, model mice + bay leaves extract group (35 mg/kg), P2, model mice + combined extract of celery and bay leaves group (35 mg/kg), P3. The animal group design is displayed in Graph.1. Extracts were orally administered for seven consecutive days. After the seventh day of treatment, food was withdrawn from the cages 12 h before the mice were sacrificed. Two hours after the last extracts administration, all mice were sacrificed. Whole blood samples were gathered and coagulated in room temperature approximately 1 h, and centrifuged to obtain the serum.



Graph.1 : Animal Groups Design

Ethics declaration

All authors hereby affirm that "Principles of laboratory animal care" were complied. In this investigation, all mice were safely caged to ensure their protection, preventing suffocation or mortality due to adverse conditions. Following the experiments, the sacrificed organs and bodies were sterilized and incinerated.

Data Analysis

The uric acid levels were measured using easy touch GCU meter device. Observational data were collected and analyzed statistically using the ANOVA method. P-value < 0.05 was chosen as the minimum level of significance. The post hock LSD was performed to investigate the significant differences within the treatment groups (A. Wahyuni, 2016).

RESULT AND DISCUSSION

Phytochemical screening is a qualitative analysis to investigate the secondary metabolism compounds contained. The extracts of natural materials contain various secondary metabolites expressing their biological activity that is considered to play important role in maintain health. In this study, phytochemical screening analysis was carried out using thin layer chromatography, color reactions test, foam test, and the chemical compounds contained in the extracts of celery and bay leaf as depicted in table.1 as follow:

Table.1 Phytochemical analysis for ethanol extract of celery plant and bay leaves

Secondary Metabolites Test	Types of Plants	Result	Rf	Reagent	Parameter
Flavonoid	Celery plants	+	0,56	$NaOH_{(aq)}$	yellow colour
	Bay leaves	+	0,68	$NaOH_{(aq)}$	Orange colour
Alkaloid	Celery plants	+	0,5	Dragendrof	Light green colour
	Bay leaves	+	0,7	Dragendrof	Dark green colour
Saponin	Celery plants	+	0,9	Foam Test	Stable foam, dark orange
	Bay leaves	+	3,4	Foam Test	Stable foam, black

Table.1 revealed that both celery and bay leaves contain the same type of phytochemical compounds namely flavonoids, alkaloid and saponins.

Flavonoid is natural compound that is responsible for inhibiting the formation of uric acid in the blood. Celery plant and bay leaves have been known for their antihyperuricemic activity (Mehmood et al., 2019; Yunarto, 2022). Previous study described that administration of boiled water extract of bay leaves enable to decrease the levels of uric acid averagely to become 5.39 mg/dl. In addition, treatment by administering the boiled water extract of celery to elderly people was able to lower the uric acid level becoming 5.93 mg/dl (Sri Wulandari, Hamna Vonny Lasanuddin, Nur Uyun I. Biahimo, & Andi Nuraina Sudirman, 2023)

Regarding this fact, it was suggested that bay leaves water extract is more effective in reducing uric acid levels in the elderly than celery leaf boiled water. This finding is influenced by the content of secondary metabolite within the extract that the higher flavonoid content found in Bay leaf extract than celery plant extract, in which 37.11 Quercetin equivalent (QE)/g and 16,45 equivalent (QE)/g for of flavonoid content in celery and bay leaves, respectively (Kholieqoh, Anam, & Kusrini, 2022; Pratama, 2021).

Normality test was performed to determine whether the dataset is normally distributed. Due to the total sample was less than 100, the test was carried out using Shapiro Wilk method as illustrated in table 2. Table 2 demonstrated that the dataset followed a normal distribution shown by significance value, 0.09, which was greater than 0.05 ($p>0.05$).

Table 2. Shapiro-Wilk method for normality test

Variable	Statistic	dF	Sig.
Uric acid level	0.930	24	0.099

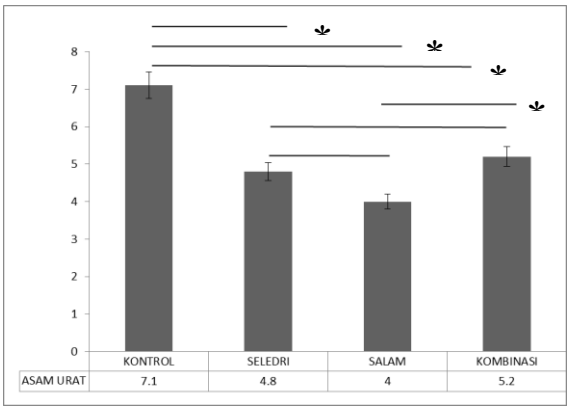
One way ANOVA test was carried out to investigate if there are statistically significant differences among the groups which displayed in Table 3 as follow:

Table 3. One Way Anova Test

Variable	N	F	Sig
Uric acid level	24	19.059	0.000

Based on one way ANOVA analysis, this study found that there is significant difference of uric acid level statistically among all the four groups, comparing one another. Four groups; P0, P1, P2, and P3 were investigated for their level of uric acid using easy touch GCU meter device. It was depicted that the uric acid level for each groups respectively; were 7.1 mg/dl, 4.9 mg/dl, 4 mg/dl and 5.2 mg/dl. P2, the administration of bay leaves extract to caffeine-induced mice model, was the most effective therapy in lowering uric acid among other groups and it was considered as the most potential antihyperuricemic agent in this finding. Furthermore, by administering celery extract, dose of 35 mg/kgBW, decreased uric acid level to be 4.8 4.9 mg/dl which was noticed as the second effective treatment in this study. These results followed the previous study regarding administering boiled water from celery leaves (*Apium graveolens L.)* to reduce uric acid values by 5.65 after being given boiled water therapy from celery leaves. These results are strengthened based on previous research on boiled water from bay leaves (*Syzygium polyanthum*) on reducing uric acid levels to 5.46 mg/dl after giving therapy (N. Wahyuni & Awaludin, 2023).

In addition, in order to investigate the significance differences of uric acid level in each group due to the administration of extract, the Post Hoc LSD test was performed as outlined in Graph.1 below. Statistical analysis using Post hoc LSD method illustrated that most of groups showed significant difference as antihyperuricemic agent. This result excluded the antihyperuricemic activity in groups of P1 compared to P3 and groups of P1 compared to P2 which showed statistically insignificant differences.



Graph 2. The difference of average uric acid in each group

*) illustrated the significant difference compared each groups

CONCLUSION

In this recent finding, the administration of extracts of celery plants, bay leaves and combination successfully lowered the level of uric acid to 4.9 mg/dl, 4 mg/dl and 5.2 mg/dl, respectively. It was noticed that the most potential antihyperuricemic activity generated by the administration of bay leaf extract (35 mg/kgBW). It was found that there are two comparison groups that did not generate the significant effectiveness in lowering uric acid, namely ethanol extract from celery compared to combination (celery + bay leaves), and celery compared to bay leaves.

Overall, our findings offer valuable insights into the effectiveness of potential activity of celery and bay leaf extract in management of hyperuricemia. These findings were carried out using easy touch GCU which might have less accuracy than spectrophotometry analysis. Further investigations, in vitro studies on the effectiveness of each extract as potential antihyperuricemic agent, in vivo studies on the inhibitory effects of each extract on xanthine oxidase and clinical trial are essential to corroborate these findings and examine the potential of these natural extracts in the development of innovative antihyperuricemic treatments

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