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Research Article

Test of Antihyperuricemia Activity of Methanol Extract of Plantain Peel (*Musa Paradisiaca* Var. Sapientum) Against *Caffeine-Induced Mice* (*Mus Musculus*)

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ABSTRACT

Background: Hyperuricemia occurs when serum uric acid levels rise above the normal range, typically exceeding 7.0 mg/dl for adults and 6.0 mg/dl for women. This condition can lead to various health issues, including gout, kidney stones, and renal failure. **Objective:** This study aims to verify the effectiveness of the methanol extract from plantain peel (Musa paradisiaca var. sapientum) in reducing uric acid levels in mice (Mus musculus) and to establish the optimal dosage for maximum efficacy. **Materials and Methods:** This analytical experimental research utilized a paired sample T-test Pretest-Posttest design. The mice were divided into five groups: a Negative Control of Na.CMC 0.5%, a Positive Control of allopurinol at 100 mg/kg body weight, and groups receiving plantain peel methanol extract at 100 mg/kg, 200 mg/kg, and 400 mg/kg body weight. Uric acid levels were measured initially, post-caffeine induction on day 7, and post-extract induction on day 14. **Results:** The study found that plantain peel methanol extract exhibited an anti-hyperuricemic effect in male mice. Among the dosages tested, 400 mg/kg body weight of the plantain peel methanol extract was the most effective in reducing uric acid levels, followed by the 200 mg/kg and 100 mg/kg doses. **Conclusion:** Plantain peel methanol extract is effective in reducing uric acid levels in male mice, with 400 mg/kg being the most efficacious dosage. This suggests potential for further exploration of plantain peels as a treatment for hyperuricemia.

Keywords: Hyperuricemia, Methanol extract, Plantain peel, Uric acid levels, Mus musculus, Optimal dosage, Anti-hyperuricemic effect.

INTRODUCTION

The accumulation of uric acid leads to joint pain, discomfort, and inflammation, making movement painful.[1] Currently, allopurinol is a prevalent pharmacological treatment for hyperuricemia, aimed at reducing uric acid levels.[2] However, this drug can cause side effects such as upper respiratory infections, diarrhea, headaches, nausea, and vomiting, which are considered adverse effects of its use.[3] Beyond synthetic drugs, natural ingredients are increasingly utilized in alternative medicine to lower uric acid levels.[4] In Indonesia, thousands of plant species and natural materials are employed for healing and disease prevention, often referred to as traditional medicinal plants, due to their minimal side effects compared to synthetic drugs. Among these, parts of the banana plant, specifically Musa acuminata colla, are recognized for their beneficial compounds like flavonoids.[5]

Commonly, only the fruit of banana plants is used, while other parts like the peel, stem, leaves, roots, and midribs are often discarded. However, plantain peels, known for their high levels of phenolic compounds compared to the fruit's flesh, are gaining attention.[6] According to Lopes *et al.*[7], plantain peels are rich in secondary metabolites such as flavonoids, saponins, terpenoids, polyphenols, and tannins. These compounds, particularly flavonoids and alkaloids, are believed to inhibit xanthine oxidase and superoxide, thereby reducing uric acid levels in the blood.[8,9]

According to Agama *et al*[10]., plantain contains various flavonoids and related compounds including quercetin, leukosianidin, 3-O-galactoside, 3-O-glucoside, and 3-O-rhamnosyl glucoside. Studies exploring the inhibitory effects of flavonoids on xanthine oxidase, such as those conducted by Hu *et al.*[11] and Huang *et al.*[12], have shown that the flavonoids quercetin and rutin effectively inhibit the xanthine oxidase enzyme, thereby reducing uric acid levels in the blood. Further research by Kibria *et al.*[13] revealed that banana peel extract contains phytochemicals like saponins, polyphenols, tannins, flavonoids, and terpenoids. The pharmacological properties of plantain peel, including antibacterial, antihyperglycemic, anti-hyperlipidemia, and antioxidant activities, are believed to originate from its compound content, such as alkaloids, phenols, flavonoids, tannins, and saponins. Phytochemical tests on methanol fractions have shown positive results for flavonoids.[14]

Plantain peel is comprised of alkaloids, flavonoids, saponins, phenols, and tannins, all of which serve as antioxidants. Phenols, in particular, are secondary metabolites in plants known for their therapeutic effects such as antimutagenic, antioxidant, anticarcinogenic activities, free radical scavenging, and reduction of cardiovascular complications. The research conducted by Sitti Raudhotul Jami'ah et al.[15]

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on the antioxidant activity of plantain peel methanol extract (*Musa paradisiacas*) indicates that the plantain peel extract possesses notable antioxidant activity, demonstrated by an IC50 value of 46.82 ppm. This underscores the significant role of secondary metabolites, particularly those with antioxidant properties.[16]

Given the numerous potential metabolite compounds found in plantain plants, particularly the antioxidant compounds that play a crucial role in combating degenerative diseases, the author is motivated to conduct pioneering research on plantain peel methanol extract. This interest stems from the lack of existing studies on the effects of reducing hyperuricemia levels through the administration of plantain peel ethanol extract, particularly using the caffeine induction method.

MATERIALS AND METHODS

This research is an experimental analytical study with a pretest-posttest design, utilizing grouped test animals. The study involves the following phytochemical screenings:

Alkaloid test

0.5 grams of extract dissolved in 1 ml of HCl 2N and 9 ml of water, divided into three parts. A positive result for alkaloids is indicated by the formation of a white (or yellowish-white) precipitate with Mayer's reagent, a brown precipitate with Wagner's reagent, and a red-orange precipitate with Dragendorff's reagent.[17]

Saponin test

0.5 grams of extract were added to a test tube with 10 ml of hot water, and shaken for 10 minutes. The persistence of foam after the addition of HCl 2N indicates a positive result for saponins. [17]

Tanin test

Extract mixed with 10 ml of hot water and shaken, then 20 ml of 10% NaCl added and filtered. The addition of FeCl3 resulting in a dark blue or black color change indicates the presence of tannins. [17]

Triterpenoid test

5 ml of extract mixed with 2 ml of chloroform and 3 ml of concentrated sulfuric acid. A brownish-red color formation between layers indicates the presence of triterpenoids. [17]

Flavonoid test

0.5 grams of extract added to ethanol, then several drops of concentrated HCl. The formation of a red color indicates the presence of flavonoids, and an orange color indicates flavone compounds.[17]

Polyphenol test

1 ml of extract solution reacted with a 10% iron (III) chloride solution. The presence of dark blue, blackish blue, or greenish-black color indicates polyphenolic compounds. [17]

Antihyperuricemia testing

Mice made hyperuricemic by six consecutive days of caffeine induction (except the negative control). On the 7th day, the uric acid levels of all groups of mice were measured. Each group received daily treatment for 7 days, and blood collection was done from the tail vein on a test strip.[18]

Test animals are categorized into five distinct groups, as follows

Group (-): Received 0.5% Na-CMC suspension (serving as the negative control group).

Group 1: Received a suspension of the extract at a dosage of 100 mg/kg body weight.

Group 2: Received a suspension of the extract at a dosage of 200 mg/kg body weight.

Group 3: Received a suspension of the extract at a dosage of 400 mg/kg body weight.

Group (+): Received Allopurinol suspension at a dosage of 100 mg/kg body weight

(serving as the positive control group).

Test samples are administered orally once daily using a gavage needle. The measurement of total cholesterol levels is conducted on days 0 (before treatment) and subsequently on days 7 and 14 (post-treatment).

Data Analysis

The data collected from the study were analyzed using the SPSS software, employing the paired sample T-Test for both pretest and posttest. The data is deemed significant if the p-value is less than 0.05.

RESULTS

This study was conducted to identify the effectiveness of natural compounds found in the peel of plantain bananas as an alternative treatment for hyperuricemia. Methanol extract from the plantain peel was administered to mice, which had been previously induced with caffeine to elevate uric acid levels. The results detailing the extract's effectiveness in reducing uric acid levels and its potential as a treatment for hyperuricemia are elucidated through the following analysis.

Univariate Analysis

The exploration of the potential of Musa paradisiaca var. sapientum (plantain banana peel) as a source of bioactive compounds was carried out through extraction using 96% methanol as the solvent to obtain phytochemical compounds from the dried plantain peel. The quantity of the extraction process is presented in Table 1.

Table 1 shows that the initial weight of the dried plantain banana peel (dry Simplicia) was 1047.5 grams. Following the extraction process, 78 grams of thick extract was obtained, indicating an extract yield of 7.44%. This yield reflects the efficiency of methanol solvent in extracting the desired compounds from the plantain banana peel. The extract yield of the plantain banana peel was then subjected to phytochemical screening to identify various bioactive compounds. The results of the phytochemical screening of the bioactive compounds from the plantain banana peel are presented in Table 2.

Table 2 reveals that there are six phytochemical groups detected in the plantain banana peel extract: Alkaloids, Saponins, Tannins, Triterpenoids, Flavonoids, and Polyphenols. Each compound was tested for its presence and confirmed through color changes, as presented in Table 2. The color changes in this table indicate the presence of active compound compositions potentially offering various health benefits.

To understand the impact of the plantain banana peel extract (Musa paradisiaca var. sapientum) on hyperuricemia, the uric acid levels in mice were measured before and after hyperuricemia induction through caffeine as presented in Table 3.

The table above presents data on the effects of caffeine and plantain banana peel extract (Musa paradisiaca var. sapientum) on uric acid levels in the body. Uric acid is a waste product found in the blood, which at high concentrations can cause gout and other health issues. Following the induction of caffeine at a dose of 100 grams/kg body weight, the uric acid levels in male mice (Mus musculus) showed a significant elevation. This induction by caffeine has been observed to elevate uric acid levels beyond the normal range, which typically lies between 8.18 and 9.6 mg/dl. Subsequent data from the study indicate that, from day 7 to day 14, there was a reduction in uric acid levels

Table 1. The result of soaking methanol extract of plantain peel *Musa paradisiaca* var. sapientum).

Sample	Solvent	Dry Simplisia (g)	Extract Thick (g)	Soaking Extract (%)
Plantain peel	Methanol 96%	1047,5	78	7,44

Table 2. Phytochemical screening results of plantain peel (*Musa paradisiaca* Var. sapientum).

No	Compound	Result (+/-)	Description
1.	Alkaloid	Positive (+)	There are chelate-colored deposits
2.	Saponin	Positive (+)	There is foam
3.	Tannin	Positive (+)	The dark blue color is formed
4.	Triterpenoid	Positive (+)	There is a red ring
5.	Flavonoid	Positive (+)	Formed orange color
6.	Polivenol	Positive (+)	Formed blue-black color

Table 3. Average uric acid levels before and after caffeine induction and plantain peel extract (*Musa paradisiaca* var. sapientum).

Group	Average uric acid levels (mg/dl) ± SD		
	Beginning of Fasting (Day 0)	Caffeine induction (Day 7)	Group dosing (Day 14)
K(-)	3,38±0,35	8,34±0,88	8,18±0,72
K(+)	3,54 ±0,29	9,06 ±0,55	3,54±0,35
K1	3,66±0.50	8,18±1,38	7,06 ±1,62
K2	3,26±0.25	9,02±0,25	7.44±0,70
K3	3,48±0.53	8,66±1,03	5,24±0,65

Table 4. The percentage result of reducing mouse uric acid (*Mus musculus*).

No	Treatment Group	Percent Decrease (%)
1	Negative Control (-)	3
2	Positive control (+)	61
3	Extract Dosage: 100 mg	14
4	Extract Dosage: 200 mg	18
5	Extract Dosage: 400 mg	40

Table 5. Results of descriptive analysis of T-test.

T-Test pretest and posttest test statistics		
Group	Treatment	Mean
Negative control	*pretest*-negative group	8,3400
	postest-negative group	9,1800
Positive control	*pretest*-positive group	9,0600
	postest-positive group	3,5400
Dosage: 100 mg	*pretest*-dose 100	8,1800
	postest-dose100	7,0600
Dosage: 200 mg	*pretest*-dose 200	9,0200
	postest-dose 200	7,4400
Dosage: 400 mg	*pretest*- dose 400	8,6600
	postest-dose 400	5,2400

in various treatment groups. Specifically, the K(+) treatment group, which received 100 mg of allopurinol (a positive control), along with the K1 group treated with 100 mg of the extract suspension, the K2 group treated with 200 mg of the extract suspension, and K3 group treated with 400 mg of the extract suspension, all showed a decrease in uric acid levels. Conversely, the K(-) treatment group, which served as the negative control and received Na-CMC, experienced a significant increase in blood sugar levels. This observation underscores the potential of caffeine induction to significantly modulate uric acid levels and the efficacy of various treatments in managing these levels.

To determine the effectiveness of plantain banana peel extract in reducing uric acid levels, an experiment was conducted using mice (Mus musculus) aimed at observing the percentage decrease in uric acid levels as presented in Table 4.

Observations from Table 4 indicate that the reduction in uric acid levels in the negative control (-) was 3%, while in the positive control (+) there was a significant reduction of 61% in uric acid levels. Treatment with plantain banana peel doses showed varying percentages of reduction; a dose of 100 mg of plantain banana peel extract resulted in a 14% decrease in uric acid levels, a 200 mg dose resulted in an 18% decrease, and a 400 mg dose demonstrated a 40% decrease in uric acid levels. These findings suggest that the plantain banana peel extract treatment is effective in reducing uric acid levels in mice (Mus musculus).

Bivariate Analysis

The effectiveness of reducing uric acid levels was assessed through bivariate analysis using the T-test. The results of the T-test analysis will provide insights into whether the reduction in uric acid occurred as a result of the intervention carried out. The descriptive analysis results compare the average values of pretest and posttest across various groups, including the negative control, positive control, and three treatment dose levels of 100 mg, 200 mg, and 400 mg, as presented in Table 5.

The descriptive analysis results of the T-Test pretest-posttest in Table 5 indicate a significant difference between the pretest and posttest values in the negative, positive, and various dosage groups. This change is significant with a p-value indicating a strong level of significance. In the negative control group, an increase in the average value of uric acid levels was observed, indicating no therapeutic effect. Conversely, the positive control and all dosage groups showed a decrease in the average post-test uric acid levels, which is likely due to the effect of the royal banana peel extract. Specifically, higher doses of royal banana peel extract correlate with a more significant reduction in average uric acid levels.

To determine the effectiveness of using royal banana peel methanol extract on the reduction of uric acid levels, results are presented in

Table 6. Test Results T-Test pretest-postest.

Uji T-Test pretest-postest			
Treatment	Mean	Significant P value	Information
Pretest-negative group *Postest*-negative group	-,84000	0,005	Significantly different
Pretest-positive group *Postest*-positive group	5,52000	0,000	Significantly different
Pretest-dose 100 *Postest*-dose100	1,12000	0,001	Significantly different
Pretest-dose 200 *Postest*-dose 200	1,58000	0,003	Significantly different
Pretest-dose 400 *Postest*-dose 400	3,42000	0,005	Significantly different

Table 7. Anova test results.

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
Decrease in uric acid levels	Between Groups	93.642	4	23.411	27.876	0.000
	Within Groups	16.796	20	.840		
	Total	110.438	24			

Table 6. The T-Test pretest-posttest results show a significant difference ($P < 0.05$) in all treatments, namely the negative group, positive group, and different dosage groups (100, 200, and 400).

Based on the table above, it is indicated that the most effective dose compared to the positive control is achieved at a 400 mg/kg body weight dosage of Musa spp. peel extract, with an average decrease in uric acid levels of 3.42000. This is also evident from the results of the variance analysis in Table 7, which indicates a significant difference in each of the tested data, and the 400 mg/kg body weight dose is the most optimal compared to the 100 mg/kg and 200 mg/kg body weight doses.

Based on Table 7, it is shown that there is a very significant decrease in uric acid levels with a p-value of <0.000. This indicates that the treatment using the extract of Musa spp. peel is effective in reducing uric acid levels.

DISCUSSION

The screening results confirm that plantain peel is positive for flavonoid compounds, saponins, tannins, and alkaloids. This finding aligns with the research conducted by Arawande *et al.*[19, 25], which indicated the presence of flavonoids, saponins, phenols, and tannins in the ethyl acetate extract of plantain peel.

The study involved the initial weighing of mice, followed by a 12-hour fasting period with only water provided, before treatment administration as per Zhang *et al.*[20] Caffeine-induced hyperuricemia is attributed to caffeine being a xanthine derivative alkaloid containing methyl compounds that oxidize to form uric acid, as noted by Bae.[21] Following 7 days of caffeine induction (100 mg/kg body weight), the mice's uric acid levels were measured again. The treatment groups included a negative group (0.5% Na-CMC suspension), a positive group (allopurinol 100 mg/kg body weight), and three dosage groups of plantain peel methanol extract at 100 mg/kg, 200 mg/kg, and 400 mg/kg body weight, respectively.

The study found an increase in uric acid levels in male mice after caffeine injection. Initially, uric acid levels ranged from 3.26-3.54 mg/dl, which rose to between 8.34 mg/dl and 9.36 mg/dl on the 7th day post-caffeine induction. Typically, caffeine is administered orally to induce hyperuricemia in mice, as stated by Kusuma *et al.*[18] Before the development of hyperuricemia, blood was drawn from the mice for baseline uric acid levels, typically collected from the tail. Once hyperuricemia was established, the mice were treated with antihyperuricemic agents including allopurinol as a positive control and plantain peel extract (*Musa paradisiaca* var. sapientum).

Both allopurinol and plantain peel methanol extract were expected to reduce uric acid levels, and the study confirmed their efficacy. The reduction in the allopurinol group is attributed to its mechanism of inhibiting the xanthine oxidase enzyme, thereby reducing uric acid formation and inhibiting purine synthesis, as discussed by Kusuma [18]. Plantain peel extract reduces uric acid levels due to its antioxidant properties, which reduce oxidative stress and inflammation, thereby affecting uric acid synthesis.[22] Additionally, the presence of phenolic compounds such as flavonoids and tannins, particularly quercetin, contributes to inhibiting xanthine oxidase activity, thus reducing uric acid levels.[23, 28]

The T-test pretest and post-test results indicated a significant decrease ($P < 0.05$) in uric acid levels with the use of plantain peel methanol extract as an antihyperuricemic in male mice (Mus musculus). The most effective dose in reducing uric acid levels was the 400 mg/kg body weight suspension of plantain peel extract, compared to the 100 mg/kg and 200 mg/kg doses. The presence of flavonoid compounds and other active components like quercetin, leukosianidin, 3-0 galactoside, 3-0-glucoside, and 3-0 rhamnosyl glucoside in plantain peels, plays a crucial role in inhibiting xanthine oxidase enzyme activity, thereby reducing blood uric acid levels.[24, 26, 27]

CONCLUSION

The study's results determined that the methanol extract of plantain peel (Musa paradisiaca var. sapientum) exhibits anti-hyperuricemia properties by effectively lowering uric acid levels in male mice (Mus musculus). The effects were noted at dosages of 100 mg/kg body weight, 200 mg/kg, and 400 mg/kg, with the results showing statistical significance ($P < 0.05$) in paired sample T-tests, both in pretest and posttest comparisons. Among the dosages tested, the 400 mg/kg body weight dosage of plantain peel extract suspension was identified as the optimal dose for anti-hyperuricemia activity in male mice, demonstrating a greater efficacy in reducing uric acid levels compared to dosages of 100 mg/kg and 200 mg/kg of the same extract.

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