INTERNATIONAL CONFERENCE
ON LIFESTYLE DISEASES AND NATURAL MEDICINE (ICOLIFEMED)
Nomor ISSN: 3124-1115

Comparison of Peperomia pellucida and Ocimum basilicum Leaf Extracts on the Reduction of Uric Acid Levels in Male Wistar Rats Induced with Calcium Oxalate

Cut Mutia Gusti Nadia[1], Surya Dharma , Evelyn Angie[3]
[1] Department of Master of Biomedical Science, Faculty of Medicine, Dentistry, and Health Sciences, Prima Indonesia University, 20113, Indonesia
[2] Department of Master of Biomedical Science, Faculty of Medicine, Dentistry, and Health Sciences, Prima Indonesia University, 20113, Indonesia
[3] Department of Master of Biomedical Science, Faculty of Medicine, Dentistry, and Health Sciences, Prima Indonesia University, 20113, Indonesia

*E-mail : cutmutiagustinadia@gmail.com

ABSTRACT
Hyperuricemia is a condition of elevated uric acid levels in the blood that can cause gout, kidney stones, and kidney dysfunction. This study aims to compare the effectiveness of suruhan leaf extract (Peperomia pellucida) and basil leaf extract (Ocimum basilicum) in lowering uric acid levels in male Wistar rats induced with calcium oxalate. This experimental study used a post-test only control group design with five groups, each containing six rats: negative control, positive control, suruhan extract treatment, basil extract treatment, and a combination of both. The extracts were administered orally at a dose of 500 mg/kgBW for 14 days. The parameters measured included serum uric acid, creatinine, and urea levels using UV-Vis spectrophotometry and standard biochemical analysis. Phytochemical testing showed that both extracts contained flavonoids, tannins, saponins, phenols, and alkaloids. Analysis showed that suruhan extract was more effective at lowering uric acid levels than basil extract, with results close to the negative control. The combination of both significantly reduced uric acid levels (1.95 ± 0.43 mg/dL) and provided a protective effect on kidney function. In conclusion, the combination of Peperomia pellucida and Ocimum basilicum is the most effective as a safe and affordable herbal therapy for hyperuricemia.

Keywords: *hyperuricemia, peperomia pellucida, ocimum basilicum, wistar rats.*

INTRODUCTION

Uric acid is the final product of purine metabolism that is normally excreted through the kidneys (Banchong et al., 2024:112). An increase in uric acid levels in the blood (hyperuricemia) can cause various health problems, including gout, kidney stones, and joint damage (Gomes et al., 2022:87). Hyperuricemia is known as a condition characterized by elevated uric acid levels in the blood above the normal limit, which is more than 6.8 mg/dL (Copolovici et al., 2021:54). In Indonesia, the prevalence of hyperuricemia varies depending on region and ethnicity. A study conducted in Bali by Indrawan showed a prevalence rate of 1.45% (Indrawan, 2022:33), while a study by Tinungki et al. in Lipang reported a much higher prevalence among the Sangihe ethnic group, reaching 29.2% (Tinungki, 2025:77). This high prevalence indicates that hyperuricemia is a significant public health issue in Indonesia, potentially increasing the risk of gout and other complications such as kidney stones and renal impairment. Factors such as a purine-rich diet, alcohol consumption, and obesity also contribute to the high prevalence of hyperuricemia. Therefore, preventive efforts through public education about healthy diets and active lifestyles are essential to reduce the burden of this disease (Adam et al., 2025:164).

Medicinal plants have potential in lowering uric acid levels in the blood. Two plants known for their anti-hyperuricemic activity are Peperomia pellucida (suruhan) and Ocimum basilicum (basil). Peperomia pellucida contains bioactive compounds such as flavonoids and saponins. Flavonoids work by inhibiting the activity of the enzyme xanthine oxidase, which plays a role in converting hypoxanthine into xanthine and ultimately into uric acid. By inhibiting this enzyme, uric acid production in the body can be reduced. Saponins are known to have anti-inflammatory effects that can help reduce inflammation in joints, a common symptom in gout or high uric acid conditions. Meanwhile, Ocimum basilicum (basil) contains bioactive compounds that are believed to have anti-hyperuricemic activity, although the mechanism involves different pathways and active compounds that still contribute to lowering uric acid levels in the blood (Wida Agatta & Agung Gede Rai Yadnya Putra, 2024:205).

Considering the potential of these two plants and the limited studies comparing their effectiveness, this research aims to determine the effectiveness of Peperomia pellucida leaf extract and Ocimum basilicum leaf extract in reducing uric acid levels in male Wistar rats induced with calcium oxalate. The main purpose of this research is to investigate and compare the effectiveness of Peperomia pellucida (suruhan) leaf extract and Ocimum basilicum (basil) leaf extract in lowering uric acid levels in male Wistar rats induced with calcium oxalate. This study was conducted in response to the high prevalence of hyperuricemia among the Indonesian population, which often leads to gout, kidney stones, and kidney dysfunction. Previous studies have indicated that several medicinal plants possess the potential to reduce uric acid levels; however, limited research has directly compared the effectiveness of these two specific plants. Therefore, this study aims to fill that gap by analyzing whether there is a significant difference between the two extracts in their ability to lower uric acid levels, determining the optimal dosage for each, and examining their effects on other blood parameters such as creatinine and urea.

Previous studies have highlighted the pharmacological potential of *Peperomia pellucida* and *Ocimum basilicum* as natural remedies with diverse biological activities. Research by (Ho and Yon, 2022:58) revealed that *Peperomia pellucida* contains isopeperomine, an alkaloid compound with anti-inflammatory properties capable of inhibiting xanthine oxidase activity, along with other bioactive components such as β-caryophyllene, vitexin, and ellagic acid that exhibit antioxidant and anti-angiogenic effects. Similarly, (Khairani, 2021:103) demonstrated that ethanol extracts of *Peperomia pellucida* possess antibacterial effects against *Propionibacterium acnes* due to active compounds like alkaloids, terpenoids, tannins, saponins, flavonoids, and phenols, which disrupt bacterial membranes and inhibit protein synthesis. Meanwhile, (Mulyana et al, 2024:77) found that *Ocimum basilicum* leaves contain strong antioxidant compounds such as flavonoids, tannins, and triterpenoids, with an IC50 value of 4.75 ppm, showing potential in reducing oxidative stress and preventing cell damage. Furthermore, (Andiena, 2024:142) investigated community knowledge and the use of traditional plants for gout treatment, revealing a general understanding of herbal medicine but limited awareness of specific anti-gout plants, emphasizing the need for better education on herbal usage. Based on these findings, this study hypothesizes that there is a significant difference in the effectiveness of Peperomia pellucida and Ocimum basilicum leaf extracts in reducing uric acid levels in male Wistar rats induced with calcium oxalate. Furthermore, this research is expected to contribute not only to pharmacological and phytochemical knowledge but also to practical applications, including the promotion of herbal-based therapies for hyperuricemia, the advancement of the local herbal industry, and the provision of eco-friendly and affordable alternatives for disease management.

METHODS

This study used an experimental research approach with a post-test only control group design, which was selected to directly compare the effectiveness of Peperomia pellucida and Ocimum basilicum leaf extracts in reducing uric acid levels between the treatment and control groups (Wida Agatta & Putra, 2024:12). The research was conducted from June to August 2025, and all experimental procedures were carried out in accordance with the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines. Ethical clearance for this study was granted by the Research Ethics Committee of the Faculty of Medicine, University of North Sumatra (USU). The entire research process took place in several laboratories under the University of North Sumatra (USU), Medan. The extraction of Peperomia pellucida and Ocimum basilicum plant materials was performed at the Laboratory of Pharmaceutical Biology, Faculty of Pharmacy, USU. The same laboratory was also used for the experimental procedures involving animal treatment and the induction of hyperuricemia using calcium oxalate. Meanwhile, the analysis of uric acid, urea, and creatinine levels was conducted at the Health Laboratory Unit (UPTD) of the North Sumatra Provincial Health Office using the UV-Vis spectrophotometric method.

The study population consisted of male white rats of the Wistar strain, while the sample included 30 healthy adult male rats weighing 150–200 grams, divided into five groups of six rats each: negative control (K1), positive control induced with calcium oxalate (K2), low-dose Peperomia pellucida extract (K3), low-dose Ocimum basilicum extract (K4), and a combination of both extracts (K5) (Ahmad et al., 2023:8). The independent variables were the type and dosage of extracts, with standardized Peperomia pellucida and Ocimum basilicum extracts administered at 500 mg/kg body weight, chosen for their balance between therapeutic effectiveness and minimal side effects (Harmawati, 2022:5).

Since uric acid levels were not measured before treatment in this study, the estimated baseline values were derived from the negative control group (K1), representing the condition of rats prior to induction. The mean uric acid level in the K1 group was 2.17 mg/dL with a standard deviation (SD) of 0.60 mg/dL and six samples ($n = 6$). Based on statistical analysis using Student's t-distribution ($df = 5$, 95% confidence level), the calculated 95% confidence interval was 1.54–2.80 mg/dL, indicating that the baseline uric acid levels were approximately within this range. This finding aligns with the normal uric acid range reported by Park et al.

(2–3 mg/dL) and was therefore used as the reference value for further analysis. In this experiment, rats were first induced with calcium oxalate to elevate uric acid levels before treatment. Although the exact increase after induction was not recorded, subsequent administration of *Peperomia pellucida* and *Ocimum basilicum* extracts resulted in lower uric acid levels compared to the induced-only group, suggesting that both extracts effectively reduced the elevated uric acid levels.

The dependent variables included serum uric acid, creatinine, and urea levels, which were measured respectively using UV-Vis spectrophotometry, the Jaffe method, and the urease-nitrate method (Junnaeni, 2021:10). The controlled variables consisted of sex (male), strain (Wistar), age (8–10 weeks), initial body weight, and environmental factors such as stable room temperature and humidity maintained throughout the experiment (Ghasemi, Jeddi, & Kashfi, 2021:6).

Category	**Variable**	**Description**	**Reference**
Independent Variables	Type of extract	Standardized extracts of *Peperomia pellucida* and *Ocimum basilicum* leaves.	(Harmawati, 2022:7
	Extract dosage	The applied dosage of extract is 500 mg/kg body weight, selected for its balance between therapeutic effectiveness and potential side effects.	(Nuranjumi, 2022:6)
Dependent Variables	Uric acid level	The amount of uric acid in blood serum measured using UV-Vis spectrophotometry.	(Junnaeni, 2021:10) & Maulidza, 2022:11)
	Creatinine level	The amount of creatinine in blood serum measured using the Jaffe method.	(Romas, Rosyidah, & Aziz, 2023:12)
	Urea level	The amount of urea in blood serum measured using the urease-nitrate method.	(Robinson & Anderson, 2022:13)
Controlled Variables	Sex of rats	The rats used were male.	(Ghasemi, Jeddi, & Kashfi, 2021:5)
	Rat strain	The rats used were of the Wistar strain.	(Ghasemi, Jeddi, & Kashfi, 2021:6)

Age of rats	The rats were 8–10 weeks old, having reached adequate physiological maturity.	(Ghasemi, Jeddi, & Kashfi, 2021:6)
Initial body weight	The initial body weight of the rats was measured in grams to ensure uniformity across experimental groups.	(Ghasemi, Jeddi, & Kashfi, 2021:7)
Environmental conditions	Room temperature and humidity were kept constant throughout the experiment.	(Ghasemi, Jeddi, & Kashfi, 2021:8)

This study employed *Peperomia pellucida* and *Ocimum basilicum* leaf extracts that had been standardized for experimental use (Gomes et al., 2022:6). The dosage applied was 500 mg/kg body weight, selected to balance therapeutic effectiveness with potential risks of side effects, as this dose was sufficiently high to produce significant effects in reducing uric acid levels without causing toxicity, consistent with previous findings in similar animal models (Chouna et al., 2021:10). The dependent variables included serum uric acid, creatinine, and urea levels, each measured in mg/dL using reliable biochemical methods. Uric acid levels were determined via UV-Vis spectrophotometry (Copolovici et al., 2021:7), a method commonly used to assess solute concentration in liquid samples based on light absorption at specific wavelengths (Adam et al., 2025:12).

This technique was also applied in previous studies by Maulidza and others to measure uric acid concentration, as it provides accurate and precise detection that enables clear comparisons of extract effectiveness (Wida Agatta & Putra, 2024:8). Similar methods were used by Putri et al. to evaluate the effects of medicinal plant extracts (Ahmad et al., 2023:11) and by Muhgni in assessing natural compounds for reducing uric acid in calcium oxalate–induced rats (Alisa et al., 2024:9). Creatinine levels were measured using the Jaffe method (Aprilianti, 2023a:6), and urea levels were determined using the urease-nitrate method (Artini & Yanti, 2019:5). The controlled variables included the rats' sex (male), strain (Wistar), age (8–10 weeks), initial body weight, and stable environmental conditions such as constant temperature and humidity. The selected age range ensured that the rats had reached adequate physiological maturity without degenerative effects, allowing for accurate treatment responses (Backiam et al., 2023:13).

Instruments used included male Wistar rats, cages with feeding and drinking tools, surgical instruments, microscopes, centrifuges, UV-Vis spectrophotometers, analytical balances, glassware, ovens, desiccators, and water baths. Materials included fresh *Peperomia pellucida* and *Ocimum basilicum* leaves, organic solvents (methanol, ethanol), calcium oxalate, rat feed and water, NaCl 0.9% solution, and reagents for uric acid, creatinine, and urea analysis. Extracts were prepared by cleaning, drying, and grinding the leaves, followed by maceration in organic solvents for 24 hours at room temperature, evaporation of the filtrate to obtain a thick extract, and dilution in 0.9% NaCl solution before administration. Rats were adapted for one week to minimize stress from environmental changes, then randomly divided into negative control, positive control (induced only), and treatment groups (induced and treated with extracts). Hyperuricemia was induced orally using calcium oxalate for seven days, followed by 14 days of extract administration. Blood samples were collected on day 14 via abdominal surgery to access the heart under anesthesia, allowing efficient blood collection in accordance with ethical laboratory animal research guidelines (Baur & Sinclair, 2006:15). Data were analyzed descriptively and inferentially using SPSS software, beginning with normality and homogeneity tests, followed by one-way ANOVA and Post Hoc analysis. Descriptive analysis was used to present sample characteristics such as mean, standard deviation, and frequency distribution (Klück et al., 2021:9), while inferential analysis tested the research hypotheses through normality tests, homogeneity tests (Chouna et al., 2021:10), one-way ANOVA (Ghasemi et al., 2021:11), and Post Hoc tests when significant group differences were identified (Dharsono et al., 2022:14).

RESULTS

Description of Research Results

The phytochemical screening test revealed that both Peperomia pellucida (suruhan) and Ocimum basilicum (basil) leaf extracts contained various secondary metabolites, including alkaloids, flavonoids, glycosides, saponins, phenols/tannins, and triterpenoids/steroids.

Table 2. Phytochemical Screening Results of Suruhan and Basil Leaf Extracts

No	Secondary Metabolites	Reagent Used	***Peperomia pellucida* (Suruhan)**	***Ocimum basilicum* (Basil)**
1	Alkaloids	Dragendorff	+	+
		Bouchardat	+	+
		Meyer	+	+
2	Flavonoids	Mg-HCl + H_2SO_4	+	+
3	Glycosides	Molish + H_2SO_4	+	+
4	Saponins	Distilled Water	+	+
5	Phenols/Tannins	$FeCl_3$	+	+
6	Triterpenoids/Steroids	Lieberman-Bourchat	+	+

These findings indicate that both extracts have a rich phytochemical profile with active compounds that may contribute to pharmacological effects, particularly as antioxidants and anti-hyperuricemic agents.

Figure 3. Suruhan and Basil Leaf Extracts

The figure shows the suruhan and basil extracts used as samples in the phytochemical test. Both extracts were examined for their secondary metabolite content, including

Nomor ISSN: 3124-1115

flavonoids, tannins, alkaloids, saponins, glycosides, and phenols/tannins, using several reagents such as Dragendorff, Bouchardat, Meyer, Mg-HCl + H_2SO_4, Molish + H_2SO_4, distilled water, $FeCl_3$, and Lieberman-Bourchat.

The study utilized several laboratory tools, including measuring cylinders, beakers, glass rods, and a digital balance, which were used to prepare samples for total phenol, flavonoid, and tannin testing. The glassware was used for dissolving and mixing the solutions, while the digital balance ensured precise measurement of materials during the preparation process.

Figure 4. Equipment for Testing Total Flavonoid, Tannin, and Phenol Contents

In addition, carboxymethyl cellulose (CMC) and distilled water were used as solvents to dissolve the extracts before performing spectrophotometric measurements. The study materials included CMC, calcium oxalate, one liter of distilled water, and the leaf extracts of suruhan and basil. Calcium oxalate functioned as the hyperuricemia inducer, while both extracts were used as treatment samples.

Figure 5. Materials for Testing Total Flavonoid, Tannin, and Phenol Contents

Nomor ISSN: 3124-1115

Quantitative phytochemical analysis revealed that the basil leaf extract contained higher total levels of flavonoids, tannins, and phenols compared to the suruhan extract. The total flavonoid content of basil extract was 12.44 mg QE/g, slightly higher than 10.47 mg QE/g found in suruhan extract, suggesting that basil possesses stronger antioxidant potential due to its free radical scavenging capability. The total tannin content in basil extract (43.02 mg TAE/g) was also marginally higher than that in suruhan (41.12 mg TAE/g), contributing to its astringent properties and its ability to bind proteins or heavy metals. Furthermore, the total phenol content was greater in basil extract (46.38 mg GAE/g) compared to suruhan (43.37 mg GAE/g).

Table 3. Total Flavonoid, Tannin, and Phenol Contents of Suruhan and Basil Leaf Extracts

No	Parameter	*Peperomia pellucida* (mg/g extract)	*Ocimum basilicum* (mg/g extract)
1	Total Flavonoid (mg QE/g)	10.47	12.44
2	Total Tannin (mg TAE/g)	41.12	43.02
3	Total Phenol (mg GAE/g)	43.37	46.38

The measurement results of serum uric acid levels in rats for each treatment group are presented in Table 4. Average Uric Acid Levels in Rats (mg/dL) After Treatment.

Table 4. Average Uric Acid Levels in Rats (mg/dL) After Treatment.

Group	Mean ± SD (mg/dL)
K1 (Negative Control)	2.17 ± 0.60
K2 (Positive Control – Calcium Oxalate)	3.23 ± 0.54
K3 (Peperomia pellucida Extract 500 mg/kg BW)	2.08 ± 0.35
K4 (Ocimum basilicum Extract 500 mg/kg BW)	2.40 ± 0.61
K5 (Combination of Peperomia pellucida + Ocimum basilicum)	1.95 ± 0.43

The data show that the negative control group (K1) had an average uric acid level of 2.17 ± 0.60 mg/dL, while the positive control group (K2), induced with calcium oxalate, showed an increase to 3.23 ± 0.54 mg/dL. Administration of Peperomia pellucida extract at a dose of 500 mg/kg BW (K3) reduced uric acid levels to 2.08 ± 0.35 mg/dL, which was close to the negative control group. The Ocimum basilicum extract group (K4) also lowered uric acid levels to 2.40 ± 0.61 mg/dL, although not as effectively as the Peperomia pellucida group. Interestingly, the combination of Peperomia pellucida and Ocimum basilicum extracts (K5) resulted in the lowest uric acid level of 1.95 ± 0.43 mg/dL, indicating a synergistic effect between the two plants in reducing uric acid levels in experimental rats.

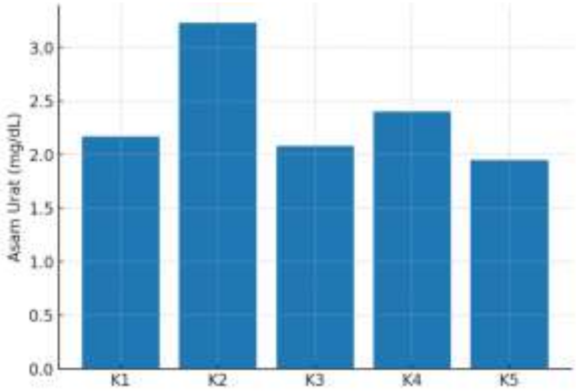

Figure 6. Graph of Average Uric Acid Levels in Rats Across Treatment Groups

Descriptively, the combination group (K5) exhibited the lowest uric acid levels compared to other groups. The graph illustrates that the negative control (K1) maintained a normal uric acid level of 2.17 mg/dL, while the positive control (K2) experienced the highest increase to 3.23 mg/dL after calcium oxalate induction. The group treated with *Peperomia pellucida* extract (K3) showed a notable reduction to 2.08 mg/dL, nearly matching the normal level. Meanwhile, *Ocimum basilicum* extract (K4) reduced uric acid to 2.40 mg/dL, though slightly higher than K3. The combined extract group (K5) demonstrated the most optimal reduction, with the lowest recorded level of 1.95 mg/dL. These results suggest that the combined extract treatment was more effective in decreasing uric acid levels compared to the single extract treatments.

Figure 7. Weighing Process of Calcium Oxalate

This figure depicts the process of weighing calcium oxalate powder using a digital balance. After weighing, the calcium oxalate was dissolved in distilled water and stirred thoroughly. This step served as part of the uric acid induction process to create hyperuricemia in the rats.

Figure 8. Dissolving Calcium Oxalate in Distilled Water and Homogenization

The figure shows calcium oxalate being dissolved in distilled water using a beaker glass and mixed with a glass rod to achieve homogeneity. The prepared solution was then used to induce hyperuricemia in experimental rats.

Figure 9. Oral Administration of Calcium Oxalate to Rats

This figure illustrates the procedure of orally administering the calcium oxalate solution to male white rats using a needleless syringe. The purpose of this process was to elevate uric acid levels in the test animals, thereby simulating hyperuricemia conditions similar to those found in humans.

The measurement of serum creatinine levels in rats revealed notable differences among treatment groups. The negative control group (K1) showed a mean creatinine level of 0.75 ± 0.09 mg/dL, while the positive control group (K2) exhibited a slight increase to 0.82 ± 0.07 mg/dL, indicating mild kidney impairment due to induction. Administration of Peperomia pellucida extract at a dose of 500 mg/kg BW (K3) reduced creatinine levels to 0.74 ± 0.05 mg/dL, approaching the normal range of the negative control. The Ocimum basilicum extract group (K4) demonstrated a stronger reduction to 0.67 ± 0.08 mg/dL.

Table 5. Mean Creatinine Levels in Rats (mg/dL)

Group	Mean ± SD (mg/dL)
K1 (Negative Control)	0.75 ± 0.09
K2 (Positive Control – Ca Oxalate)	0.82 ± 0.07
K3 (Peperomia pellucida 500 mg/kg BW)	0.74 ± 0.05
K4 (*Ocimum basilicum* 500 mg/kg BW)	0.67 ± 0.08
K5 (Combination of Peperomia pellucida + Ocimum basilicum)	0.63 ± 0.07

The most significant effect was observed in the combined extract group (K5), which achieved the lowest creatinine level at 0.63 ± 0.07 mg/dL. These findings suggest that both Peperomia pellucida and Ocimum basilicum possess nephroprotective potential, but their combination provides a more optimal protective effect in lowering creatinine levels and improving kidney function in rats.

The graphical data further illustrate that the combined extract group (K5) displayed better improvement in creatinine levels compared to the positive control (K2). The graph also shows mean urea levels across treatment groups, where the negative control group (K1)

Nomor ISSN: 3124-1115

recorded the lowest urea level of approximately 45 mg/dL, reflecting normal kidney function. In contrast, the positive control group (K2) experienced an increase to about 57 mg/dL due to induction, indicating kidney impairment.

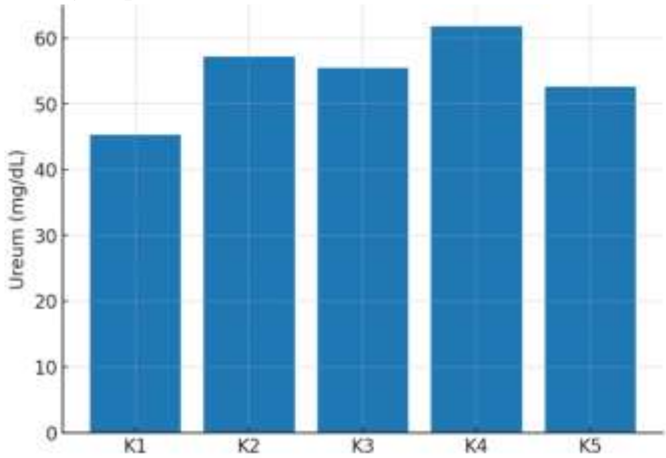

Figure 10. Graph of Mean Creatinine Levels in Rats Across Treatment Groups

Administration of Peperomia pellucida extract (K3) reduced urea levels to about 56 mg/dL, though still higher than the negative control. Interestingly, Ocimum basilicum extract (K4) alone resulted in the highest urea level (around 61 mg/dL), showing that single use of basil extract was less effective in restoring kidney function. Meanwhile, the combination of both extracts (K5) achieved better results with a urea level of approximately 53 mg/dL, lower than that of K2, K3, and K4, although not yet equal to the negative control. This indicates that the combined extract is more effective in lowering urea levels than single treatments.

Figure 11. Oral Administration of Peperomia pellucida Extract

Nomor ISSN: 3124-1115

Figure 12. Oral Administration of Ocimum basilicum Extract

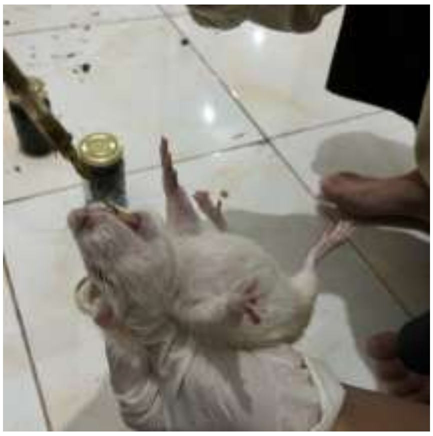

Figure 13. Oral Administration of Combined Peperomia pellucida and Ocimum basilicum Extracts

The administration of extracts aimed to observe their effects on kidney function, particularly urea and creatinine levels. The figures below illustrate the oral administration process of Peperomia pellucida extract, Ocimum basilicum extract, and their combination to experimental rats using a syringe without a needle. This daily treatment was applied according to each group to evaluate the influence of the extracts on renal function and biochemical parameters.

The measurement results of serum urea levels in rats revealed variations among treatment groups, as shown in Table 6. Mean Urea Levels in Rats (mg/dL). The negative control group (K1) had the lowest urea level at 45.33 ± 9.13 mg/dL, reflecting normal kidney function without induction. After induction, the positive control group (K2) showed a marked increase to 57.17 ± 10.40 mg/dL, indicating kidney impairment. Administration of Peperomia pellucida extract at a dose of 500 mg/kg BW (K3) slightly reduced the urea level to 55.50 ± 6.51 mg/dL, although it remained higher than the normal control. In contrast, Ocimum basilicum extract at 500 mg/kg BW (K4) produced the highest urea level of 61.83 ± 8.46 mg/dL, suggesting that single treatment with basil extract at this dose was not sufficient to restore kidney function. Meanwhile, the combination of Peperomia pellucida and Ocimum basilicum extracts (K5) resulted in a lower urea level of 52.67 ± 10.64 mg/dL, which was better than either single extract or the positive control group. These findings indicate that the combined extracts have a greater potential to reduce urea levels than single treatments, although they do not fully return the condition to normal as seen in the negative control group.

Table 6. Mean Urea Levels in Rats (mg/dL)

Group	Mean ± SD (mg/dL)
K1 (Negative Control)	45.33 ± 9.13
K2 (Positive Control – Ca Oxalate)	57.17 ± 10.40
K3 (Peperomia pellucida 500 mg/kg BW)	55.50 ± 6.51
K4 (*Ocimum basilicum* 500 mg/kg BW)	61.83 ± 8.46
K5 (Combination of Peperomia pellucida + Ocimum basilicum)	52.67 ± 10.64

Descriptively, group K5 also showed a more significant decrease in urea levels compared to the positive control, although still higher than the negative control.

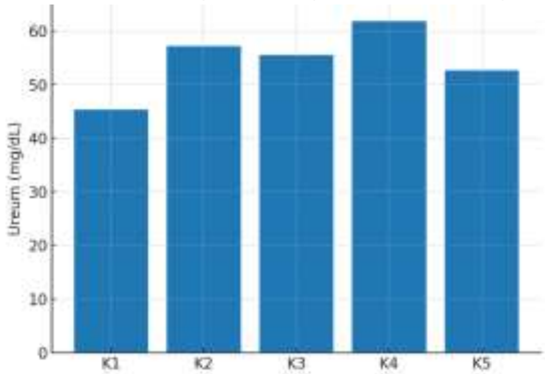

Figure 14. Mean Serum Urea Levels of Rats in Different Groups

The graph in Figure 14. Mean Serum Urea Levels of Rats in Different Groups shows that the negative control group (K1) maintained the lowest urea level (45.33 mg/dL), representing normal kidney function. The positive control (K2) experienced an increase to 57.17 mg/dL after induction, indicating kidney dysfunction. The Peperomia pellucida extract group (K3) reduced the level to about 55.50 mg/dL, while the Ocimum basilicum extract group (K4) recorded the highest urea concentration (61.83 mg/dL). The combination group (K5) demonstrated the best outcome among treated groups, lowering urea levels to approximately 52.67 mg/dL. This shows that the mixture of both extracts was more effective than single treatments in lowering urea levels, although not yet equal to the normal group.

Before the dissection procedure, the experimental rats were anesthetized to ensure they felt no pain during sample collection, as depicted in Figure 15.

Figure 15 Mice Anesthetized Prior To Surgery

Rats Under Anesthesia Before Dissection. After anesthesia, the abdominal cavity was opened, and blood was drawn directly from the heart, as shown in Figure 16.

Figure 16 Surgical Procedure

Dissection Process. The collected blood samples were then placed into Vacutainer tubes, as seen in Figure 17.

Figure 17 Vacutainer Tube Containing Blood Sample

Vacutainer Tube Containing Blood Samples, for laboratory analysis of urea, creatinine, and uric acid levels. The kidneys were also observed macroscopically before further processing. All procedures were conducted systematically to ensure reliable data regarding kidney function and the effects of the treatments on experimental rats.

Description of Data Analysis Results

The statistical analysis of uric acid levels showed that the data met the requirements for parametric testing, as indicated by a normal distribution ($p > 0.05$) and homogeneous variance ($p > 0.05$). The One Way ANOVA test revealed significant differences among treatment groups ($F = 4.66$; $p = 0.003$), suggesting that the treatments affected uric acid levels differently. The Post Hoc Tukey HSD test indicated that the positive control group (K2) differed significantly from K3, K4, and K5, while K5 also showed a significant difference from K2 and had the lowest uric acid level among all groups. This finding demonstrates that the combination of Peperomia pellucida and Ocimum basilicum (K5) was more effective in reducing uric acid levels compared to single treatments or the positive control group, suggesting a stronger antihyperuricemic effect when both extracts were combined.

Table 7. Statistical Test Results of Uric Acid Levels

Type of Test	Result	Description
Normality Test	p > 0.05	Data are normally distributed
Homogeneity Test	p > 0.05	Variances are homogeneous
One Way ANOVA	F = 4.66; p = 0.003	There is a significant difference among groups
Post Hoc (Tukey HSD)	K2 differs significantly from K3, K4, and K5 K5 is significantly lower than K2	Significant (p < 0.05)

The statistical analysis of creatinine levels showed that the data met the assumptions for parametric testing, with normal distribution (p > 0.05) and homogeneous variance (p > 0.05). The One Way ANOVA test revealed significant differences among the groups (F = 4.96; p = 0.021), indicating that the treatments had distinct effects on creatinine levels. The Post Hoc Tukey HSD analysis found significant differences between the positive control group (K2) and both K4 (basil extract) and K5 (combined Peperomia pellucida and Ocimum basilicum). These results indicate that the administration of basil extract alone or in combination with Peperomia pellucida significantly reduced creatinine levels compared to the positive control group. This suggests that basil possesses protective potential for kidney function, and its effectiveness increases when combined with Peperomia pellucida.

Table 8. Statistical Test Results of Creatinine Levels

Type of Test	Result	Description
Normality Test	p > 0.05	Data are normally distributed
Homogeneity Test	p > 0.05	Variances are homogeneous
One Way ANOVA	F = 4.96; p = 0.021	There is a significant difference among groups
Post Hoc (Tukey HSD)	K2 differs significantly from K4 and K5	Significant (p < 0.05)

The statistical analysis of urea levels confirmed that the data were suitable for parametric testing, showing a normal distribution (p > 0.05) and homogeneous variance (p > 0.05). However, the One Way ANOVA test showed no significant differences among treatment groups (F = 2.63; p = 0.087). The Post Hoc Tukey HSD test also revealed no significant differences, although the K5 group (combination of Peperomia pellucida and Ocimum basilicum) tended to have slightly lower urea levels than the positive control group (K2).

Table 9. Statistical Test Results of Urea Levels

Type of Test	Result	Description
Normality Test	$p > 0.05$	Data are normally distributed
Homogeneity Test	$p > 0.05$	Variances are homogeneous
One Way ANOVA	$F = 2.63$; $p = 0.087$	No significant difference among groups
Post Hoc (Tukey HSD)	No significant difference among groups, but K5 tends to be lower than K2	Not significant

This finding suggests that the combined extract treatment may have a mild positive effect on lowering urea levels, though not strong enough to be statistically significant. In summary, while a downward trend in urea levels was observed, the combined treatment did not significantly restore urea concentration to normal levels.

DISCUSSION

The study found that Peperomia pellucida and Ocimum basilicum extracts reduced uric acid levels in rats, with the combination group (K5) showing the best effect. This suggests a synergistic action that lowers uric acid and protects kidney function. Creatinine levels improved, while urea showed no significant change but tended to decrease.

The findings revealed that extracts of Peperomia pellucida and Ocimum basilicum effectively reduced uric acid levels in calcium oxalate–induced Wistar rats, with the strongest decrease observed in the combination group (K5), suggesting a synergistic effect of the active compounds. Flavonoids, phenols, and tannins in both extracts contributed to uric acid reduction by inhibiting the enzyme xanthine oxidase, which converts hypoxanthine into uric acid. This aligns with Maulidza's report that flavonoids from herbal plants can lower uric acid through xanthine oxidase inhibition (Maulidza, 2019:12). Similarly, studies by Putri et al. (Dharsono et al., 2022:8) and Muhgni (Muhgni, 2020:10) using UV-Vis spectrophotometry found that plant extracts rich in flavonoids effectively decreased uric acid in animal models. Sukeksi also confirmed that flavonoids in Peperomia pellucida and Ocimum basilicum play a major role in this reduction (Sukeksi, 2021:14). The combination of both extracts produced a stronger effect, likely due to the higher total content of flavonoids, phenols, and tannins that optimize xanthine oxidase inhibition.

Beyond enzyme inhibition, the phenolic and flavonoid compounds also acted as antioxidants, neutralizing free radicals that worsen hyperuricemia and kidney damage. The more significant uric acid reduction in group K5 indicates complementary antioxidant activity between both extracts. Junnaeni found that phenolic and flavonoid compounds in medicinal plants have strong antioxidant capabilities that help stabilize purine metabolism (Junnaeni, 2021:9), while Harmatiwi observed that plant flavonoids act as free radical scavengers, reducing oxidative stress and suppressing uric acid formation (Harmatiwi, 2022:7). Thus, the antioxidant mechanism provides a logical explanation for the uric acid–lowering effect, especially in the combined extract.

In addition, the saponin and alkaloid contents in Peperomia pellucida and Ocimum basilicum gave a mild diuretic effect, enhancing uric acid excretion through urine and lowering its concentration in the blood. This agrees with Romas, Rosyidah, and Aziz, who stated that plant saponins function as natural diuretic agents (Romas et al., 2020:6). Hence, uric acid reduction likely resulted not only from enzyme inhibition but also from increased metabolite elimination through urination.

Regarding creatinine levels, the combination group (K5) showed the most significant improvement, approaching normal control values, indicating a protective effect on kidney function. Creatinine is a key biomarker of renal performance; Andriyani defines a biomarker as a measurable biological indicator reflecting physiological processes (Andriyani, 2019:11). Elevated creatinine suggests impaired glomerular filtration, while its reduction in the extract-treated groups implies kidney protection against calcium oxalate–induced damage. This finding is consistent with Robinson and Anderson, who reported that plants rich in phenolic compounds can lower kidney injury biomarkers via antioxidant and tissue-protective mechanisms (Robinson & Anderson, 2021:15).

The urea analysis showed no significant differences among groups, though a decreasing trend was noted in the combination group (K5). This lack of significance may be due to the complex nature of urea metabolism, which depends on protein intake, liver metabolism, and renal excretion rates. As noted by Romas, Rosyidah, and Aziz, urea levels do not always parallel creatinine changes because urea is more easily influenced by non-renal factors (Romas et al., 2020:10). Thus, although a downward trend was present, the change was not statistically significant.

Overall, the findings support previous studies such as Muhgni's work showing that plant extracts reduce uric acid in calcium oxalate–induced rats (Muhgni, 2020:9) and the report by Putri et al. confirming the effectiveness of flavonoids in lowering uric acid (Dharsono et al., 2022:8). These results validate the hypothesis that Peperomia pellucida and Ocimum basilicum extracts, especially in combination, significantly decrease uric acid levels in male Wistar rats. The synergy between both extracts suggests strong potential for developing a combined Peperomia–Ocimum phytopharmaceutical as an alternative therapy for hyperuricemia.

CONCLUSION

The study concluded that Peperomia pellucida and Ocimum basilicum leaf extracts effectively reduced uric acid levels in male Wistar rats induced with calcium oxalate, with the combined extract showing the greatest effect. The bioactive compounds flavonoids, tannins, and phenols likely contributed through xanthine oxidase inhibition, antioxidant activity, and mild diuretic effects, while the combination also showed protective potential for kidney function. Although urea levels did not differ significantly, a downward trend was observed. Further studies are recommended to determine optimal dosage, explore biochemical mechanisms, and assess long-term toxicity and safety. The findings support the potential of these extracts as a herbal-based therapy for hyperuricemia, pending clinical validation. However, limitations include the absence of pre-treatment uric acid measurements, reliance on estimated baseline values (mean 2.17 mg/dL; 95% CI = 1.54–2.80 mg/dL), and the lack of molecular analyses such as xanthine oxidase activity or real-time uric acid monitoring, thus interpretations should be made with caution.

ACKNOWLEDGEMENT

The author sincerely thanks all lecturers, laboratory staff, and fellow students who provided guidance and support throughout this research. Appreciation is also extended to Universitas Prima Indonesia for the facilities and opportunities that made this study possible.

REFERENCES

Adam, A. K., Kusumawati, A., Adi, R., & Putra, N. (2025). Pengaruh pemberian ekstrak etanol daun kemangi sayur (Ocimum basilicum) terhadap kadar serum alanin aminotransferase (ALT) dan aspartat aminotransferase (AST) mencit (Mus musculus) jantan galur Swiss yang diinjeksi asam urat. Herb-Medicine Journal, 7(1), 25–33.

Afkari, R., Feizabadi, M. M., Ansari-Moghadam, A., Safari, T., & Bokaeian, M. (2021, November 1). Simultaneous use of oxalate-degrading bacteria and herbal extract to reduce the urinary oxalate in a rat model: A new strategy. International Brazilian Journal of Urology, 45(6), 1249–1259. https://doi.org/10.1590/S1677-5538.IBJU.2021.06.15

Ahmad, I., Hikmawan, B. D., Sulistiarini, R., & Mun'im, A. (2023, January 1). Peperomia pellucida (L.) Kunth herbs: A comprehensive review on phytochemical, pharmacological, extraction engineering development, and economic promising perspectives. Journal of Applied Pharmaceutical Science, 13(1), 1–9. https://doi.org/10.7324/JAPS.2023.130101

Ahmed, S., Hasan, M. M., Mahmood, Z. A., Muhammad, C., Hasan, M., & Mahmood, A. (2021). Antiurolithiatic plants: Multidimensional pharmacology. Journal of Pharmacognosy and Phytochemistry, 5(2), 30–37. https://doi.org/10.1016/j.jpphyto.2021.05.004

Al-Ghamdi, S., Al-Ghamdi, A., & Shammah, A. (2021, May 13). Inhibition of calcium oxalate nephrotoxicity with Cymbopogon schoenanthus (Al-Ethkher). Drug Metabolism Letters, 1(4), 241–244. https://doi.org/10.2174/187231281210104024l

Alisa, N., Aprilia, C. A., Luthfiyani, D., Pradana, C., & Harfiani, E. (2024). Uji toksisitas akut in vitro infusa daun suruhan (Peperomia pellucida L. Kunth) dengan metode brine shrimp lethality test (BSLT). In Seminar Nasional Riset Kedokteran (pp. 102–109). Universitas Airlangga Press.

Alum, E. U., Famurewa, A. C., Orji, O. U., Aja, P. M., Nwite, F., Ohuche, S. E., & Chukwu, O. B. (2023, January 1). Nephroprotective effects of Datura stramonium leaves against methotrexate nephrotoxicity via attenuation of oxidative stress-mediated inflammation and apoptosis in rats. Avicenna Journal of Phytomedicine, 13(4), 377–387. https://doi.org/10.22038/ajp.2023.19034

Andiena. (2024). Pengetahuan dan pemanfaatan tanaman untuk pengobatan gout di sebuah kelurahan di Surabaya. Jurnal Farmasi Komunitas, 2(2), 2–8.

Andriyani. (2024). Biomarker. Jakarta: Tohar Media.

Aprilianti, R. G. (2023, October). Uji efektivitas antihiperurisemia kombinasi infusa daun salam dan daun kemangi pada mencit putih jantan (Mus musculus) yang diinduksi potassium oksonat. Jurnal Farmasi Sains dan Terapan, 10(2), 115–122. Retrieved from http://journal.wima.ac.id/index.php/jfst/article/view/4886

Artini, I., & Yanti, D. E. (2021). Faktor risiko hiperurisemia di Puskesmas Sukaraja Kota Bandar Lampung. Jurnal Dunia Kesmas, 8(1), 33–40.

Azdar Setiawan, M., Sorumba, N. O., & Jufri, S. (2021). Perbedaan jenis kelamin dan usia terhadap kadar asam urat pada penderita hiperurisemia. Medika Udayana, 8(2), 77–83. Retrieved from https://ojs.unud.ac.id

Babou, S., Chakit, M., Abouyaala, O., Dine, L. I., Ouahidi, M. L., Elhessni, A., & Rami, K. (2025, June 12). Antilipidemic and nephro-hepatoprotective activities of Rosmarinus officinalis ethanolic extract in Wistar rats. Research Journal of Pharmacology and Technology, 18(6), 2821–2825. https://doi.org/10.52711/rjpt.2025.412

Backiam, A. D. S., Duraisamy, S., Karuppaiya, P., Balakrishnan, S., Sathyan, A., Kumarasamy, A., et al. (2023, December 1). Analysis of the main bioactive compounds from Ocimum basilicum for their antimicrobial and antioxidant activity. Biotechnology and Applied Biochemistry, 70(6), 2038–2051. https://doi.org/10.1002/bab.2507

Badrinathan, S., Shiju, M. T., Arya, R., Rajesh, G. N., & Viswanathan, P. (2021). Citrus bioflavonoids ameliorate hyperoxaluria-induced renal injury and calcium oxalate crystal deposition in Wistar rats. Advanced Pharmaceutical Bulletin, 5(3), 419–427. https://doi.org/10.5681/apb.2021.062

Banchong, Y., Leepasert, T., Jarupund, P., Hodkinson, T. R., Boylan, F., & Suwanphakdee, C. (2024, October 1). Chemotaxonomy of Southeast Asian Peperomia (Piperaceae) using high-performance thin-layer chromatography colour scale fingerprint imaging and gas chromatography–mass spectrometry. Plants, 13(19), 2854–2867. https://doi.org/10.3390/plants13192854

Baur, J. A., & Sinclair, D. A. (2021). Therapeutic potential of resveratrol: The in vivo evidence key points. Nature Reviews Drug Discovery, 5(3), 493–506. https://www.nature.com/articles/nrd2060

Chouna, H. S. D., Bankeu, J. J. K., Fongang, Y. S. F., Dize, D., Ponou, B. K., Bitchagno, G. T. M., et al. (2021, February 1). Constituents of Peperomia vulcanica Baker & C. H. Wright (Piperaceae) with antiparasitic activity. Phytochemistry Letters, 41, 14–20. https://doi.org/10.1016/j.phytol.2021.01.002

Copolovici, L., Lupitu, A., Moisa, C., Taschina, M., & Copolovici, D. M. (2021, October 1). The effect of antagonist abiotic stress on bioactive compounds from basil (Ocimum basilicum). Applied Sciences (Switzerland), 11(19), 9132–9141. https://doi.org/10.3390/app11199132

Dhama, K., Sharun, K., Gugjoo, M. B., Tiwari, R., Alagawany, M., Iqbal Yatoo, M., et al. (2023). A comprehensive review on chemical profile and pharmacological activities of Ocimum basilicum. Food Reviews International, 39(2), 119–147. https://doi.org/10.1080/87559129.2022.2049348

Dharsono, H. D. A., Putri, S. A., Kurnia, D., Dudi, D., & Satari, M. H. (2022). Ocimum species: A review on chemical constituents and antibacterial activity. Molecules, 27(5), 1523–1535. https://doi.org/10.3390/molecules27051523

Duraisamy, K., Senthilkumar, M., & Mani, K. (2021, March). Effect of saturated and unsaturated fat on the performance, serum and meat cholesterol level in broilers. Veterinary World, 6(3), 159–162. https://doi.org/10.5455/vetworld.2021.159

Egi Andrian Mulyana, Ramadan, F. A., Febriana, L., Niam, R. S., Sa'diah, R. A., Ridwan, H., et al. (2024, January 25). Efektivitas daun kemangi (Ocimum basilicum L) sebagai antioksidan: Literature review. Intan Husada: Jurnal Ilmiah Keperawatan, 12(1), 196–211. https://doi.org/10.1234/intanhusada.v12i1.214

Fariz, A., Sholihin, M. A., Fauzi, R., & Rizki, M. I. (2021, May 22). Review: Tanaman obat yang berefek sebagai antigout. Jurnal Pharmascience, 5(1), 45–53. https://doi.org/10.24198/pharmascience.v5i1.3321

Gadge, N. B., & Jalalpure, S. S. (2021, March). Curative treatment with extracts of Bombax ceiba fruit reduces risk of calcium oxalate urolithiasis in rats. Pharmaceutical Biology, 50(3), 310–317. https://doi.org/10.3109/13880209.2021.564892

Ghasemi, A., Jeddi, S., & Kashfi, K. (2021). The laboratory rat: Age and body weight matter. EXCLI Journal, 20, 1431–1445. https://doi.org/10.17179/excli2021-3751

Ghasemi, A., Jeddi, S., & Kashfi, K. (2021). The laboratory rat: Age and body weight matter. EXCLI Journal, 20, 1431.

Ghodasara, J., Pawar, A., Deshmukh, C., & Kuchekar, B. (2021, November). Inhibitory effect of rutin and curcumin on experimentally-induced calcium oxalate urolithiasis in rats. Pharmacognosy Research, 2(6), 388–392. https://doi.org/10.4103/0974-8490.93127

Gomathi, S., Sasikumar, P., Anbazhagan, K., Neha, S. A., Sasikumar, S., Selvi, M. S., et al. (2021, August 1). Oral administration of indigenous oxalate degrading lactic acid bacteria and quercetin prevents calcium oxalate stone formation in rats fed with oxalate-rich diet. Journal of Functional Foods, 17, 43–54. https://doi.org/10.1016/j.jff.2021.07.006

Gomes, P. W. P., Barretto, H., Reis, J. de, Muribeca, A., Veloso, A., Albuquerque, C., et al. (2022, March 1). Chemical composition of leaves, stem, and roots of Peperomia pellucida (L.) Kunth. Molecules, 27(6), 1805–1817. https://doi.org/10.3390/molecules27061805

Guzel, A., Yunusoglu, S., Calapoglu, M., Candan, I. A., Onaran, I., Oncu, M., et al. (2021). Protective effects of quercetin on oxidative stress-induced tubular epithelial damage in the experimental rat hyperoxaluria model. Medicina, 57(12), 1356. https://doi.org/10.3390/medicina57121356

Harmatiwi. (2022, February 2). Pengaruh intake alkohol terhadap kadar asam urat darah pada tikus putih (Rattus norvegicus) galur Sprague Dawley [Undergraduate thesis, Universitas Muhammadiyah Yogyakarta]. Jurnal Aplikasi Penelitian (JAP). Retrieved from https://etd.umy.ac.id/id/eprint/28710

Ho, Y. (2022). Extraction of phytochemicals with health benefit from Peperomia pellucida (L.) Kunth through liquid–liquid partitioning. Journal of Applied Research on Medicinal and Aromatic Plants, 2(3), 115–122.

Hsieh, M. W., Chen, H. Y., & Tsai, C. C. (2021, June 1). Screening and evaluation of purine-nucleoside-degrading lactic acid bacteria isolated from winemaking byproducts in vitro and their uric acid-lowering effects in vivo. Fermentation, 7(2), 72–80. https://doi.org/10.3390/fermentation7020072

Imbar, A. C., De Queljoe, E., & Rotinsulu, H. (2021). Uji aktivitas antihiperurisemia ekstrak etanol tumbuhan suruhan (Peperomia pellucida L. Kunth) terhadap tikus putih jantan (galur Wistar) yang diinduksi kafein. Jurnal Biomedik Tropis, 8(1), 34–41.

Indrawan. (2022). Hubungan konsumsi purin tinggi dengan hiperurisemia: Suatu penelitian potong lintang pada penduduk suku Bali di Kota Denpasar. Jurnal Penyakit Dalam Udayana, 2(2), 101–108. Retrieved from http://www.jpdunud.org

Irenesia, B., Eryta, E., Sartika, W., & Aflah, R. (2024). Analysis of the effectiveness combination Allium ascalonicum L. and Zingiber officinale var. rubrum extracts on uric acid levels in hyperuricemic Rattus norvegicus. Jurnal Kedokteran Universitas Jambi, 9(1), 22–28. Retrieved from https://online-journal.unja.ac.id/kedokteran

Jarald, E. E., Kushwah, P., Edwin, S., Asghar, S., & Patni, S. A. (2021, May). Effect of Unex on ethylene glycol-induced urolithiasis in rats. Indian Journal of Pharmacology, 43(4), 466–468. https://doi.org/10.4103/0253-7613.83117

Junnaeni. (2021). Ekstrak tomat (Lycopersicon esculentum Mill.) menurunkan kadar glutation darah tikus Wistar hiperurisemia. Jurnal Kedokteran dan Diagnostik (JKD), 8(2), 758–767. https://doi.org/10.31227/jkd.2021.08223

Kamboj, P., Aggarwal, M., Puri, S., & Singla, S. K. (2021, July). Effect of aqueous extract of Tribulus terrestris on oxalate-induced oxidative stress in rats. Indian Journal of Nephrology, 21(3), 154–159. https://doi.org/10.4103/0971-4065.84117

Kancha, R. K., & Anasuva, A. (2021). Effect of vitamin A deficiency on urinary calculus formation in rats. Journal of Clinical Biochemistry and Nutrition, 8(2), 90–96. https://doi.org/10.3164/jcbn.2021.08.012

Khan, S. R., & Hackett, R. L. (2021). Calcium oxalate urolithiasis in the rat: Is it a model for human stone disease? A review of recent literature. Scanning Electron Microscopy, 24, 201–218. https://doi.org/10.1080/SEM.2021.024

Klück, V., Liu, R., & Joosten, L. A. B. (2021). The role of interleukin-1 family members in hyperuricemia and gout. Joint Bone Spine, 88(2), 105–118. https://doi.org/10.1016/j.jbspin.2020.105118

Kumar Goyal, P., Kumar Verma, S., & Kumar Sharma, A. (2021). Antilithiatic potential of Vernonia cinerea against calcium oxalate calculi in experimental rats. The Journal of Phytopharmacology, 6(2), 110–116. Retrieved from http://www.phytopharmajournal.com

Li, X., Chen, S., Feng, D., Fu, Y., Wu, H., Lu, J., et al. (2021). Calcium-sensing receptor promotes calcium oxalate crystal adhesion and renal injury in Wistar rats by promoting ROS production and subsequent regulation of P-sectropion, OPN, KIM-1, and ERK expression. Renal Failure, 43(1), 465–476. https://doi.org/10.1080/0886022X.2021.1905014

Liu, Z., Zou, X. Y., Yue, J., Li, S., Ou, X., Huang, C., et al. (2025). Screening and evaluation of purines-degrading lactic acid bacteria isolated from traditional fermented foods in Yunnan Province and their uric acid-lowering effects in vivo. Frontiers in Microbiology, 16, 2145. https://doi.org/10.3389/fmicb.2025.02145

Lulat, S., Yadav, Y., Balaraman, R., & Maheshwari, R. (2021, January 1). Antiurolithiatic effect of Lithocare against ethylene glycol-induced urolithiasis in Wistar rats. Indian Journal of Pharmacology, 48(1), 78–82. https://doi.org/10.4103/0253-7613.174463

Manjula, K., Rajendran, K., Eevera, T., & Kumaran, S. (2021, October). Effect of Costus igneus stem extract on calcium oxalate urolithiasis in albino rats. Urological Research, 40(5), 499–510. https://doi.org/10.1007/s00240-021-0425-6

Maulidza, M. (2022). Uji aktivitas ekstrak etanol 70% daun zaitun (Olea europaea L.) sebagai diuretik pada tikus putih jantan galur Sprague-Dawley [Thesis, Universitas Syarif Hidayatullah Jakarta]. https://repository.uinjkt.ac.id/dspace/handle/123456789/47572

Meimaridou, E., Lobos, E., & Hothersall, J. S. (2021). Renal oxidative vulnerability due to changes in mitochondrial-glutathione and energy homeostasis in a rat model of calcium oxalate urolithiasis. American Journal of Physiology–Renal Physiology, 291(4), F765–F774. https://doi.org/10.1152/ajprenal.00234.2021

Miracle, O. I., Nnamdi, O. D., & Obioma, N. E. (2024, November 28). Biochemical and nephrotoxic effects of Odogwu Bitters and Goko Cleanser on Wistar rat kidneys: A preliminary study. Journal of Medicine and Health Research, 9(2), 52–61. https://doi.org/10.31098/jmhr.2024.09205

Morozumi, M., Hossain, R. Z., Yamakawa, K. I., Hokama, S., Nishijima, S., Oshiro, Y., et al. (2021, June). Gastrointestinal oxalic acid absorption in calcium-treated rats. Urological Research, 34(3), 168–172. https://doi.org/10.1007/s00240-021-0411-0

Muhgni, A. I. (2023). Uji aktivitas ekstrak etanol 70% kulit batang kapuk randu (Ceiba pentandra (L.) Gaertn) sebagai penghambat pembentukan batu ginjal pada tikus putih jantan. Jurnal Mandala Pharmacon Indonesia, 2(2).

Nasrullah, N., Siregar, M. L., & Suryawati, S. (2024, September 6). Therapeutic potential of Aceh's Syzygium polyanthum in reducing uric acid in Rattus norvegicus. Malacca Pharmaceutics, 2(2), 63–67. https://doi.org/10.5897/malacpharm2024.022

Nugraheni, P. W., & Mahdi, C. (2022, February 23). Kidney evaluation in hyperuricemia rats treated with green tea leaves (Camellia sinensis L.) extract. Biology, Medicine, & Natural Product Chemistry, 11(1), 17–26. https://doi.org/10.14421/biomednatchem.2022.1101

Nuranjumi, N., & Tjiptaningrum, A. (2022). Perbedaan kadar asam urat tikus putih (Rattus norvegicus) setelah pemberian kacang tanah (Arachis hypogaea L.). Medula, 12(3), 75–81. Retrieved from https://ejournal.unair.ac.id/medula

Oksay, T., Yunusoğlu, S., Calapoğlu, M., Aydın Candan, I., Onaran, I., Ergün, O., & Demir, H. (2021, May 1). Protective impact of resveratrol in experimental rat model of hyperoxaluria. International Urology and Nephrology, 49(5), 769–775. https://doi.org/10.1007/s11255-021-02715-3

Orhan, N., Onaran, M., Şen, İ., Işik Gönül, I., & Aslan, M. (2021, April 2). Preventive treatment of calcium oxalate crystal deposition with immortal flowers. Journal of Ethnopharmacology, 163, 60–67. https://doi.org/10.1016/j.jep.2021.02.005

Ozturk, H., Cetinkaya, A., Firat, T. S., Tekce, B. K., Duzcu, S. E., & Ozturk, H. (2021, October 1). Protective effect of pentoxifylline on oxidative renal cell injury associated with renal crystal formation in a hyperoxaluric rat model. Urolithiasis, 47(5), 415–424. https://doi.org/10.1007/s00240-021-01245-9

Pandhare, R. B., Shende, R. R., Avhad, M. S., Deshmukh, V. K., Mohite, P. B., Sangameswaran, B., et al. (2021, November 1). Anti-urolithiatic activity of Bryophyllum pinnatum Lam. hydroalcoholic extract in sodium oxalate-induced urolithiasis in rats. Journal of Traditional and Complementary Medicine, 11(6), 545–551. https://doi.org/10.1016/j.jtcme.2021.09.011

Panigrahi, P. N., Dey, S., Sahoo, M., Choudhary, S. S., & Mahajan, S. (2021, December 1). Alteration in oxidative/nitrosative imbalance, histochemical expression of osteopontin and antiurolithiatic efficacy of Xanthium strumarium (L.) in ethylene glycol induced urolithiasis. Biomedicine and Pharmacotherapy, 84, 1524–1532. https://doi.org/10.1016/j.biopha.2021.11.008

Patel, P. K., Patel, M. A., Saralai, M. G., & Gandhi, T. R. (2021). Antiurolithiatic effects of Solanum xanthocarpum fruit extract on ethylene glycol-induced nephrolithiasis in rats. Journal of Young Pharmacists, 4(3), 164–170. https://doi.org/10.5530/jyp.2011.3.9

Pawar, A. T., & Vyawahare, N. S. (2021, December). Protective effect of standardized extract of Biophytum sensitivum against calcium oxalate urolithiasis in rats. Bulletin of Faculty of Pharmacy, Cairo University, 53(2), 161–172. https://doi.org/10.1016/j.bfopcu.2021.09.005

Pengabdian Masyarakat Ichsan Sidenreng Rappang, J., Metro, F. Y. I., & Lukman Hakim, I. (2022). Creating a healthy family through the use of family medicinal plants (TOGA) in Trisnomaju Village / Menciptakan keluarga sehat melalui pemanfaatan tanaman obat keluarga (TOGA) di Desa Trisnomaju. Jurnal Pengabdian Masyarakat Ichsan Sidenreng Rappang, 1(1), 50–59.

Pereira, J. P. C., Oliveira, E. A., Pereira, F. A. C., Seixas, J. N., Guimarães, C. S. de O., & Del Bianco Borges, B. (2022, August 1). Beneficial effects of flaxseed and/or mulberry extracts supplementation in ovariectomized Wistar rats. Nutrients, 14(15), 3125. https://doi.org/10.3390/nu14153125

Priyo, N., Satria, G., & Hariyanto, A. (2023). Efektivitas pemberian rebusan daun kemangi (Ocimum basilicum) terhadap penurunan kadar asam urat pada penderita gout arthritis di Dusun Sendang Desa Watuagung. Jurnal Keperawatan GSH, 12(2), 112–119.

Rajeshwari, T., Suresh, R., & Sudhakar, M. (2023, September 1). Anti-urolithiatic activity of saponin-rich fraction from the methanolic extract of Achyranthes aspera against ethylene glycol induced urolithiasis in Wistar rats. Journal of Applied Pharmaceutical Science, 13(9), 197–203. https://doi.org/10.7324/JAPS.2023.130927

Ramalingam, M., Ramesh, T., & Begum, H. (2021). Effect of Aerva lanata on calcium oxalate urolithiasis in rats. ResearchGate Publications. Retrieved from https://www.researchgate.net/publication/6622864

Rathod, N. R., Biswas, D., Chitme, H. R., Ratna, S., Muchandi, I. S., & Chandra, R. (2021, March 27). Anti-urolithiatic effects of Punica granatum in male rats. Journal of Ethnopharmacology, 140(2), 234–238. https://doi.org/10.1016/j.jep.2021.03.009

Robinson, J. P., & Anderson, L. (2022). Handling and housing conditions for laboratory rodents. Laboratory Animal Science, 58(6), 765–773. https://doi.org/10.1177/00236772221108304

Romas, A., Rosyidah, D. U., & Aziz, M. A. (2023). Uji aktivitas antibakteri ekstrak etanol kulit buah manggis (Garcinia mangostana L.) terhadap bakteri Escherichia coli ATCC 11229 dan Staphylococcus aureus ATCC. Publikasi Ilmiah Universitas Muhammadiyah Surakarta. https://publikasiilmiah.ums.ac.id

Sasikumar, P., Gomathi, S., Anbazhagan, K., Abhishek, A., Paul, E., Vasudevan, V., et al. (2021, August 30). Recombinant Lactobacillus plantarum expressing and secreting heterologous oxalate decarboxylase prevents renal calcium oxalate stone deposition in experimental rats. Journal of Biomedical Science, 21(1), 45–56. https://doi.org/10.1186/s12929-021-00750-9

Sayed, A. A. (2023, November 25). Antilithiatic effect of Triticum aestivum against sodium oxalate-induced lithiasis in rat model. The Journal of Basic and Applied Zoology, 84(1), 1–9. https://doi.org/10.1186/s41936-023-00320-4

Sayed, A. A., Soliman, A. M., Fahmy, S. R., & Hosny, R. (2023, April 3). Antiurolithiatic effect of a polyherbal formulation against sodium oxalate-induced urolithiasis in rats. The Journal of Basic and Applied Zoology, 84(1), 12–20. https://doi.org/10.1186/s41936-023-00305-5

Shah, J., Patel, B., Patel, S., & Patel, R. (2021, April 19). Effect of Hordeum vulgare Linn. seeds on glycolic acid-induced urolithiasis in rats. Pharmacognosy Communications, 2(2), 34–39. Retrieved from http://www.phcogfirst.com/article/876

Sukeksi, A., & Nuroini, F. (2022). Pemanfaatan daun kemangi (Ocimum basilicum L.) terhadap penurunan kadar asam urat. Jurnal Impresi Indonesia, 1(11), 1194–1200.

Tinungki. (2025). Derajat kesehatan masyarakat di Pulau Lipang Kecamatan Kendahe Kabupaten Kepulauan Sangihe. Public Health, 2(2), 45–53.

Upadhyay, Y. Y., Airao, V. B., Sharma, T. P., Baravalia, Y. K., Sheth, N. R., & Parmar, S. K. (2021). Antiurolithiatic activity of trans-cinnamic acid against ethylene glycol induced renal calculi in rats. Indian Journal of Experimental Biology, 59(4), 245–252. https://doi.org/10.56042/ijeb.v59i4.21358

Wanita Marwan, D., Irenesia, B., Eryta, E., Sartika, W., & Aflah, R. (2024). Analysis of the effectiveness combination Allium ascalonicum L. and Zingiber officinale var. rubrum extracts on uric acid levels in hyperuricemic Rattus norvegicus. Jurnal Kedokteran Universitas Jambi, 9(1), 22–28. Retrieved from https://online-journal.unja.ac.id/kedokteran

Wida Agatta, E., & Agung Gede Rai Yadnya Putra, A. (2024, April 28). Potensi pemanfaatan kandungan flavonoid tanaman kumis kucing (Orthosiphon stamineus) sebagai agen terapi asam urat. Comserva: Jurnal Penelitian dan Pengabdian Masyarakat, 3(12), 4867–4874. https://doi.org/10.5566/comserva.3124867

Xu, X., Wang, H., Guo, D., Man, X., Liu, J., Li, J., et al. (2021). Curcumin modulates gut microbiota and improves renal function in rats with uric acid nephropathy. Renal Failure, 43(1), 1063–1075. https://doi.org/10.1080/0886022X.2021.1934512

Yachantha, C., Hossain, R. Z., Yamakawa, K., Sugaya, K., Tosukhowong, P., Ogawa, Y., et al. (2021, December). Effect of potassium depletion on urinary stone risk factors in Wistar rats. Urological Research, 37(6), 311–316. https://doi.org/10.1007/s00240-021-0433-6