E-ISSN 2723-4959

Vol. 7 No. 1 June 2026

BIOFAAL JOURNAL

PATTIMURA UNIVERSITY

BIOFAAL JOURNAL

E-ISSN 2723-4959
Volume 7 Number 1 | June 2026

Publisher
Department of Biology, Faculty of Science and Technology, Pattimura University,
in collaboration with
The Indonesian Association of Physiology Experts

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BIOFAAL JOURNAL

Research Article

Article History:
Received : February 27, 2026
Revised : May 7, 2026
Accepted : May 15, 2026
Available online : May 29, 2026
Published : June 1, 2026

Key words:
Antihyperuricemia, clove tea bag, uric acid, *Syzygium aromaticum*,

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Cite this article:
Adrien Jems Akiles Unitly, A. J. A., Killay, A., Nindatu, M., Moniharapon, D. D., Silahooy, V. B., Sikafir, B. B., Moniharapon, M., Seimahuira, T. N., Lesbatta, J. K., Sillehu, E. S., Eddy, L & Laratmase, N. D. (2026). Phytopharmacological Potential of Clove Tea Formulation of Clove and Cinnamon As An Antihyperuricemic Agent In Hyperuricemic Rat Model. Biofaal Journal, 7(1):59-69.
https://doi.org/10.30598/biofaal.v7i1pp59-69

Phytopharmacological Potential of Clove Tea Formulation of Clove and Cinnamon as an Antihyperuricemic Agent in Hyperuricemic Rat Model

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Abstract
High-protein dietary patterns, particularly those rich in animal protein with high purine levels, may lead to hyperuricemia, characterized by elevated blood uric acid levels. This study aimed to evaluate the phytopharmaceutical activity of clove tea bags on changes in blood uric acid levels in hyperuricemic Rattus norvegicus rats. The study employed a completely randomized design consisting of five treatment groups with three replications. The groups included a negative control without potassium bromate induction or clove tea administration, a positive control induced with 29 g of potassium bromate to establish a hyperuricemia model, and three treatment groups induced with hyperuricemia followed by clove tea administration at doses of 0.23 g/tail/day, 0.35 g/tail/day, and 0.46 g/tail/day for 14 days. Data were analyzed to determine differences in blood uric acid levels among groups. The results demonstrated that clove tea administration reduced blood uric acid levels, with the most effective dose being 0.23 g/tail/day. These findings suggest that clove tea has potential as a natural therapeutic agent for managing hyperuricemia and contribute to the development of plant-based functional interventions.

INTRODUCTION

High protein dietary patterns, particularly those rich in animal protein containing high levels of purines, may contribute to the development of hyperuricemia, characterized by elevated blood uric acid levels. Increased serum uric acid levels are associated with the occurrence of gout (Ria et al., 2021, as cited in Barokah & Ramadhan, 2023). Sedentary behavior, elevated body mass index, central obesity, and increased remnant cholesterol levels have also been reported to be associated with higher serum uric acid concentrations (Chen et al., 2025; Zhou et al., 2025; Shim et al., 2025). Hyperuricemia commonly affects men over 40 years of age and postmenopausal women. Uric acid is the final product of purine metabolism

in humans. During purine metabolism, xanthine and hypoxanthine are oxidized into uric acid by the enzyme xanthine oxidase. This indicates that excessive uric acid production and or reduced uric acid excretion may lead to hyperuricemia (Anggraini, 2022).

The management of hyperuricemia generally involves medications that inhibit the activity of xanthine oxidase, thereby controlling purine catabolism in the body. The most commonly used synthetic drug is allopurinol. However, prolonged use of this medication may cause adverse effects namely kidney disorders and decreased blood cells. Therefore, alternative therapies based on traditional medicinal plants have been increasingly explored. Traditional medicines, including herbal-based preparations, have the potential to prevent and control blood uric acid levels (Purukan et al., 2020, as cited in Desmarta & Farida, 2024). In general, the main mechanism of phytochemical compounds in reducing uric acid levels is through xanthine oxidase inhibition and antioxidant activity that suppresses oxidative stress, thus supporting the potential of clove tea as a natural agent in the prevention and therapy of hyperuricemia. (Gunarti & Hidayah, 2022; Warman et al., 2025).

Clove (*Syzygium aromaticum*) is an endemic plant of the Maluku Islands, Indonesia, belonging to the family Myrtaceae within the order Myrtales (Titaley et al., 2023; Ayal et al., 2024). Clove is widely used as a culinary spice and as a traditional remedy for various diseases. Its distinctive aroma is primarily attributed to eugenol, the main bioactive compound (72-90%), which exhibits strong antioxidant properties. Eugenol also possesses antiseptic and anesthetic effects (Laghari & Khan, 2022). Clove essential oil demonstrates pharmacological activities, including anesthetic, antimicrobial, antiseptic, antioxidant, and immunomodulatory effects. Additionally, phenolic compounds in clove leaves contribute to antioxidant activity, while flavonoids function as free radical scavengers (Laratmase & Nindatu, 2019).

Empirically, cloves (*Syzygium aromaticum*) have long been used to treat stomach aches, eye disorders, loss of appetite, and colic, and are consumed as a decoction to help overcome high uric acid levels because they contain flavonoid alkaloids, saponins, and tannins which are antioxidants. The novelty of this study lies in the development of a tea formulation combining cloves and cinnamon (*Cinnamomum* sp.), both of which exhibit antihyperuricemic effects (Wang et al., 2023). This is because both have rich antioxidant content, so it is expected to provide scientific evidence supporting their potential as natural therapeutic agents and contribute to the development of functional foods that target oxidative stress-related degenerative diseases. Therefore, this study aims to evaluate the phytopharmaceutical potential of clove tea as an antihyperuricemic agent in a rat model of hyperuricemia.

RESEARCH METHODS

Research Design

This study employed a quantitative experimental approach using a completely randomized design. A total of 15 male white rats (*Rattus norvegicus*), aged 8 weeks and weighing approximately 200 g, were randomly divided into five treatment groups, with three replications in each group.

Time and Location of the Study

The research was conducted from August 5 to November 18, 2025, at the Zoology Laboratory, Faculty of Science and Technology, Pattimura University.

Instruments and Materials

The instruments used in this study included a digital weighing scale, animal cages, drinking bottles, feeding bowls, an oral gavage needle, a uric acid measuring device (Easy Touch GCU), tea bag sachets, and a hot plate. The materials consisted of male white rats (*Rattus norvegicus*), clove, cinnamon, cotton, aluminum foil, distilled water, uric acid test strips, antiseptic solution, standard laboratory feed, potassium bromate, and rice husk bedding.

Research Variables

The study consisted of two variables: the independent variable and the dependent variable. The independent variable was the administration of clove tea bags, while the dependent variable was the blood uric acid level.

Research Procedure

The first step involved the preparation of clove tea bags. A total of 200 g of dried clove buds and 100 g of dried cinnamon were blended together into a fine powder. The powdered mixture was then weighed according to the designated treatment doses and packaged into tea bag sachets.

The second step Phytochemical analysis of clove tea, was conducted in the Basic Chemistry Laboratory, Faculty of Science and Technology, Pattimura University. The third step consisted of grouping the experimental animals. The rats were divided into five treatment groups with three replications each: a negative control group that did not receive potassium bromate induction or clove tea administration; a positive control group induced with 29 g potassium bromate to establish a hyperuricemia model (Laratmase & Nindatu, 2019); treatment group P1, in which hyperuricemic rats were administered clove tea at a dose of 0.23 g/tail/day for 14 days; treatment group P2, which received 0.35 g/tail/day for 14 days; and treatment group P3, which received 0.46 g/tail/day for 14 days. Doses P1, P2, and P3 are obtained from the conversion of clove tea use in hyperuricemia therapy in humans:

Table 1. Comparison of body weight of experimental animals for dose conversion follows the Laurence and Bachrah conversion table of 1964.

	20g Mice	**200g Rat**	**400g Guinea pig**	**1,5kg Rabbit**	**2,0kg Cat**	**4,0kg Ape**	**12,0kg Dog**	**70,0kg Human**
20 g Mice	1,0	7,0	12,25	27,8	29,7	64,1	124,2	387,9
200 g Rat	0,14	1,0	1,74	3,9	4,2	9,2	17,8	56,0
400 g Guinea pig	0,08	0,57	1,0	2,25	2,4	5,2	10,2	31.5
1,5 kg Rabbit	0,04	0,25	0,44	1,0	1,08	2,4	4,5	14,2
2,0 kg Cat	0,03	0,23	0,41	0,92	1,0	2,2	4,4	13,0
4,0 kg Ape	0,016	0,11	0,19	0,42	0,45	1,0	1,9	6,1

	20g Mice	**200g Rat**	**400g Guinea pig**	**1,5kg Rabbit**	**2,0kg Cat**	**4,0kg Ape**	**12,0kg Dog**	**70,0kg Human**
12,0 kg Dog	0,008	0,06	0,10	0,22	0,24	0,52	1,0	3,1
70,0 kg Human	0,0026	0,018	0,031	0,07	0,076	0,16	0,32	1,0

The conversion factor for humans weighing 70 kg to rat weighing ± 200 g is 0.018. The average weight of Indonesians is 50 kg. The dose of clove tea given to humans in the treatment of hyperuricemia is 18 g per day, consumed in three doses (morning, noon, and evening), so that each dose is 6 g. Furthermore, to determine the dose in test animals (mice), the dose conversion from humans to animals is carried out using the formula:

= Indonesian body weight/European body weight × human use dose × conversion value

= 50/70 × 18 g × 0.018 = 0.71 × 18 g × 0.018

= 0.23 g

Based on the results above, a dose of 0.23 g was obtained which became dose I. Then a half-step dose was added to become the second dose, namely 0.35 g, and half was added for the third dose to become 0.46.

The Fourth step involved daily administration of clove tea according to the respective doses for 14 consecutive days. At the end of the treatment period, blood samples were collected from the rats for measurement of uric acid levels.

For the measurement procedure, the uric acid device was calibrated using the strip code key before inserting the test strip, which automatically activated the device. The code number displayed on the screen was verified to match the strip packaging code. Blood samples were obtained from the lateral tail vein of the rats and applied to the test strip. Within approximately 20 seconds, the blood uric acid level was displayed on the screen.

Data Analysis

The obtained uric acid levels were analyzed using analysis of variance (ANOVA), followed by Duncan's multiple range test at a 95% confidence level. Statistical analysis was performed using SAS software.

RESULTS AND DISCUSSION

The results of phytochemical tests on clove tea (*Syzygium aromaticum*) in this study indicate the presence of secondary metabolites in the form of alkaloids, flavonoids, terpenoids, phenolics, saponins, tannins and vitamin C. The presence of these compounds aligns with various previous studies that reported that cloves contain bioactive components such as flavonoids, alkaloids, saponins, and tannins, which play a role in their pharmacological activity (Pratama et al., 2019; Nindatu et al., 2021; Laratmase et al., 2021) (Table 2).

The presence of flavonoids, alkaloids, saponins, tannins, and terpenoids in clove tea also has the potential to provide antihyperuricemic effects through the inhibition of xanthine oxidase, an enzyme involved in uric acid formation. Several studies have shown that flavonoids such as quercetin and luteolin can inhibit xanthine oxidase activity, thereby reducing uric acid levels in the blood (Gunarti & Hidayah, 2022).

Table 2. Phytochemical content of clove tea

No	Parameter Uji / Komponen	Hasil
1	Alkaloid	+
2	Flavonoid	+
3	Terpenoid	+
4	Fenolik	+
5	Saponin	+
6	Tanin	+
7	Vitamin C	+

The results showed that the mean changes in blood uric acid levels of rats after administration of clove tea bags are presented in Table 3. Analysis of variance (ANOVA) indicated a significant reduction in blood uric acid levels during the first week among all clove tea treatment groups compared to both the negative and positive control groups ($P < 0.05$). This reduction is presumed to be associated with the phytochemical constituents of clove, which may exert their biological activity from the early phase of administration.

Table 3. Mean changes in blood uric acid levels of rats after administration of clove tea bags

Uric Acid (mg/dL)	**Clove Tea Treatment Groups**				
	K(-)	**K(+)**	**P1**	**P2**	**P3**
First Week	4.8 ±0.01^{b}	6.0±0.01^{a}	4.4±0.01^{c}	4.3±0.01^{c}	4.1 ±0.01^{d}
Second Week	4.6 ±0.01^{b}	8.5 ±0.03^{a}	4.4 ±0.02^{cb}	4.4 ±0.02^{cb}	4.0 ±0.01^{c}

Note: Different superscript letters within the same row indicate statistically significant differences among treatment groups ($P < 0.05$). K (−): negative control group that did not receive 29 g potassium bromate induction or clove tea administration. K (+): positive control group induced with 29 g potassium bromate (hyperuricemia model). P1: hyperuricemic rats treated with clove tea at a dose of 0.234 g/head/day for 14 days. P2: hyperuricemic rats treated with clove tea at a dose of 0.351 g/head/day for 14 days. P3: hyperuricemic rats treated with clove tea at a dose of 0.468 g/head/day for 14 days.

In the second week, a more pronounced effect was observed. The clove tea treatment groups (P1, P2, and P3) demonstrated significantly lower uric acid levels compared to both the negative and positive control groups ($P < 0.05$). Notably, the uric acid levels in P1, P2, and P3 were lower than those of the negative control group. These findings indicate that continuous administration of clove tea may enhance its antihyperuricemic effect over time. A progressive decrease in blood uric acid levels was observed from the first to the second week, suggesting a time-dependent therapeutic effect of clove tea.

Rats normally exhibit serum uric acid concentrations ranging from approximately 1.2 to 5.0 mg/dL (Aliyah, 2024). In the present study, the reduction in uric acid levels to 4.0 mg/dL following clove tea administration is presumed to be associated with the flavonoid content of clove. Uric acid may interact with flavonoids to form complexes, potentially altering its structure and reducing its biological activity. Flavonoids, with their hydroxyl groups and aromatic structures, can bind uric acid, forming molecular complexes that affect its conformation and reactivity. This has the potential to reduce the free uric acid fraction in biological systems, as well as affect its solubility and excretion processes, thus contributing to lower overall uric acid levels (Hasan et al., 2020).

The primary mechanism by which flavonoids reduce uric acid levels is through inhibition of the xanthine oxidase enzyme, a key enzyme responsible for converting hypoxanthine and xanthine into uric acid (Yusuf et al., 2020). This finding is consistent with previous studies indicating that flavonoids decrease uric acid levels via xanthine oxidase inhibition (Sonia et al., 2020). One of the major flavonoid aglycones with potent xanthine oxidase inhibitory activity is quercetin. Zustika et al., (2025) reported that quercetin naturally inhibits xanthine oxidase and suppresses uric acid formation, thereby alleviating gout symptoms. The molecular structure of quercetin, characterized by a double bond between C2 and C3 and five hydroxyl groups, enables it to function as both an allosteric and competitive inhibitor of xanthine oxidase. Additionally, quercetin acts as a strong antioxidant capable of neutralizing free radicals and superoxide reactions. Furthermore, quercetin is a flavonoid compound with potent antioxidant activity through its ability to donate hydrogen atoms or electrons to stabilize free radicals, including reactive oxygen species such as the superoxide radical. This mechanism allows quercetin to inhibit oxidative chain reactions, reduce oxidative stress, and protect biomolecules such as lipids, proteins, and DNA from oxidative damage.

Pathophysiologically, hyperuricemia is closely associated with oxidative stress and systemic inflammation. Increased inflammatory responses and oxidative stress contribute to enhanced uric acid synthesis and are part of the broader spectrum of metabolic and chronic inflammatory disorders (Alemayehu et al., 2023; Zhou et al., 2025; Shim et al., 2025). Therefore, the flavonoid compounds present in clove tea may reduce uric acid levels by inhibiting xanthine oxidase activity and attenuating inflammatory processes.

In addition to flavonoids, clove tea also contains vitamin C, which plays an important role as an antioxidant. Vitamin C contributes to the reduction of blood uric acid levels by acting as a free radical scavenger and suppressing oxidative stress. Adequate vitamin C intake has been reported to prevent hyperuricemia and reduce the risk of related complications, such as gout and hyperuricemic nephropathy (Heriani et al., 2022). The association between vitamin C and uric acid is linked to renal tubular reabsorption processes, particularly in the proximal tubules, where vitamin C may enhance urinary uric acid excretion. Furthermore, vitamin C contributes to the attenuation of inflammation and oxidative stress, both of which are involved in increased uric acid synthesis Mukherjee et al., (2025). This finding is consistent with Zhang et al., (2025), who reported that antioxidants play a significant role in suppressing inflammatory responses.

Hyperuricemia has been shown to activate immune responses and elevate systemic inflammatory biomarkers. Increased pan-immune-inflammatory values observed in individuals with hyperuricemia indicate the involvement of inflammatory pathways in disease progression. Persistent inflammatory conditions have also been associated with the clinical manifestations of chronic inflammatory disorders (Tabra et al., 2025). Therefore, the antioxidant activity of vitamin C present in clove tea may exert protective effects by reducing inflammation in hyperuricemic conditions, thereby contributing to decreased blood uric acid levels.

In addition to flavonoids and vitamin C, other bioactive compounds present in clove tea, including alkaloids, tannins, and saponins, may also contribute to the reduction of uric acid levels. These compounds have been reported to inhibit xanthine oxidase activity, enhance

urinary uric acid excretion, and scavenge free radicals generated during purine metabolism. This is consistent with findings by Artini et al. (2021) and Ningsih et al. (2021), who demonstrated thet alkaloids, tannins, and saponins exhibit significant antioxidant and antihyperuricemic activities in experimental animal models.

Beyond lowering uric acid levels, the antioxidant properties of these compounds have been associated with improvements in renal function and a delay in the progression of chronic kidney disease related to oxidative stress and inflammation under hyperuricemic conditions (Nie et al., 2025; Zhang et al., 2025). Therefore, the antihyperuricemic effect of clove tea may not only reduce serum uric acid levels but also provide protective effects on renal function.

As a plant-based intervention, clove tea may offer a safer long-term therapeutic alternative compared to synthetic medications, which are often associated with adverse effects (Zheng et al., 2025). In this context, the utilization of clove tea as a phytopharmaceutical preparation represents a relevant and potentially safer strategy for managing hyperuricemia compared to conventional pharmacological therapies that carry a higher risk of side effects (Al-Worafi, 2024).

Overall, the findings of this study are consistent with previous experimental research demonstrating that plant-derived bioactive compounds, including flavonoids, vitamin C, alkaloids, tannins, and saponins, are effective in reducing uric acid levels through multiple mechanisms. These mechanisms include inhibition of xanthine oxidase activity, enhancement of uric acid excretion, and suppression of oxidative stress and inflammatory responses (Hasan et al., 2020; Yusuf et al., 2020; Laratmase et al., 2021; Artini et al., 2021; Ningsih et al., 2021). Therefore, clove tea has the potential to be developed as a phytopharmaceutical and functional food applicable in the management of hyperuricemia, particularly as a natural-based adjunct therapy for long-term use.

CONCLUSION

Based on the findings of this study, the administration of clove tea significantly reduced blood uric acid levels in hyperuricemic rats. The most effective dose for lowering uric acid levels was 0.23 g/tail/day. These results indicate that clove tea has potential as a natural antihyperuricemic agent and may be considered for further development as a plant-based adjunct therapy for hyperuricemia management.

ACKNOWLEDGEMENTS

The authors express their sincere appreciation to the Zoology Laboratory, Faculty of Science and Technology, Universitas Pattimura, Ambon, Indonesia, for providing laboratory facilities and technical support that made this research possible.

DECLARATIONS

Author Contributions

N. D. L and B. B. S contributed to designing the study, preparing samples and test materials, conducting the study. K. J. L., V. B. S and E. S. S contributed to data analysis. A. J. A.U., A.K., M.

N., D. D. M., M. M., T. N. S and L E. contributed to preparing the manuscript and proofreading the manuscript.

Funding
This research received no external funding.

Declaration of Interest
The authors declare no conflict of interest.

Data Sharing Statement
The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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