Window of Health
Jurnal Kesehatan
journal homepage : www.jurnal.fkmumi.ac.id

ARTICLE RESEARCH

URL article: http://jurnal.fkmumi.ac.id/index.php/woh/article/view/woh9212

Anti-hyperuricemia Activity of Ethanol Extract of Bajakah Stem (*Spatholobus litoralis* Haask) on *In Vivo* Model: Analysis of Uric Acid and Cyclooxygenase-2 Levels

[C]Muhammad Ilyas Y[1,2], Apriyanto[3], Adriatman Rasak[4], Nirwati Rusli[5], Asriullah Jabbar[6], Ufu Rindang[7], Fadhliyah Malik[8]
[1,2,3,4,5,] Politeknik Bina Husada Kendari, Kendari, Indonesia
[2,6,7,8]Department of Pharmacy, Faculty of Pharmacy, Universitas Halu Oleo, Kendari, Indonesia
Email Correspondence Authors ([C]): ilyasyusufmuhammad.apt@gmail.com
Ilyasyusufmuhammad.apt@gmail.com[1,2], apriyantoyuni@gmail.com[3], adriatmanrasak@gmail.com[4], nirwatirusli@gmail.com[5], asriullahjabbar@uhu.ac.id[6], ufurindang@gmail.com[7], fadhliyah@uho.ac.id[8]

ABSTRACT

Investigation of bajakah (*Spatholobus littoralis* Hassk), a typical plant of the island of Borneo, as an anti-hyperuricemia and anti-inflammatory agent through the cyclooxygenase-2 (COX-2) inhibition pathway is important to reveal. This is supported by previous research indicating that bajakah has strong anti-inflammatory and antioxidant effects, with a higher flavonoid content. Evidence-based studies were conducted to determine whether the bajakah stem extract can reduce uric acid levels and inhibit COX-2 as an anti-hyperuricemia therapy. This study was conducted in vivo on mice with a hyperuricemia model induced by potassium oxonate. The treatment consisted of a normal control group, a negative control (Na-CMC, 0.5%), a positive control (allopurinol), and a dose-variation group of Bajakah stem ethanol extract at 100, 200, and 300 mg/kg BW. Uric acid levels were determined at hours 1, 2, and 3 by lateral chromatography and COX-2 levels by the sandwich ELISA method. The study results showed that bajakah stem ethanol extract in the 300 mg/kg body weight dose group was effective in reducing uric acid levels at the 3rd hour from 3.60 ± 0.25 mg/dL to 2.33 ± 0.35 mg/dL, with the greatest reduction of 0.33 ± 0.06 mg/dL, equivalent to 92%, and reduced COX-2 levels by 1.14 ± 0.02 ng/mL, which was significantly different from the negative control ($p<0.05$), and there was a positive correlation between the reduction in uric acid levels and COX-2 inhibition in hyperuricemic animal models. The conclusion of this study is that administration of bajakah wood can increase uric acid levels while simultaneously inhibiting inflammation, making it a potential candidate for development as an antihyperuricemic and anti-inflammatory drug.

Keywords: Bajakah stem; uric acid; cyclooxygenase-2, antihyperuricemia; *in vivo*

PUBLISHED BY :
Faculty of Public Health
Universitas Muslim Indonesia
Address :
Jl. Urip Sumoharjo Km. 5 (Kampus II UMI)
Makassar, Sulawesi Selatan.
Email :
jurnalwoh.fkm@umi.ac.id
Phone :
+62 82188474722

Article history
Received 5 June 2024
Received in revised 26 March 2026
Accepted 26 April 2026
Available online 2 May 2026

INTRODUCTION

Hyperuricemia is a serious health issue today that commonly affects older adults, characterized by elevated blood uric acid levels exceeding the normal threshold, which can result in increased uric acid production, reduced uric acid excretion in urine, or a combination of both.(1) Increased uric acid levels can cause several health problems in sufferers, such as a feeling of sciatica in the joint area accompanied by moderate to severe pain, inflammation, and joint disorders that can result in fatal movement disorders in several organs of the body.(2)

Uric acid has a role in modulating cyclooxygenase-2 (COX-2) levels in patients, so inflammation is often found in hyperuricemia conditions. Research conducted by Kirca et al. (2017), showed that uric acid can activate proliferation pathways in Vascular Smooth Muscle Cells (VSMC), and uric acid augmentation of VSMC proliferation in renal arteries is mediated by COX-2 and triggers inflammation and endothelial disorders.(3) Research conducted by Xu et al. (2006) showed that ERK1/2 (p44/42 MAPK) and p38 Mitogen-Activated Protein Kinase (MAPK) pathways are responsible for the uric acid-induced increase in COX-2.(4) In addition, hyperuricemia increases the production of reactive oxygen species (ROS) through the activation of NADPH oxidase and xanthine oxidase and increases the production of MCP-1 and COX-2 mRNA.(5)

Treatment of hyperuricemia with pharmacological therapy of uricostatic drugs used today, namely allopurinol as the main choice, with the mechanism of action inhibiting the formation of uric acid through inhibiting the action of the enzyme xanthine oxidase. However, long-term use of allopurinol can cause several problems such as gastrointestinal side effects (nausea, vomiting, and diarrhea), leukopenia, aplastic anemia, liver damage, interstitial nephritis, and hypersensitivity.(6)

The discovery and development of new drugs derived from natural sources are urgently needed as alternatives for the treatment of hyperuricemia/gout accompanied by inflammation. The identification of new chemical compounds from natural sources as potential drug candidates for hyperuricemia accompanied by inflammation holds great promise. This is necessary because there are currently very few antihyperuricemic drug options derived from natural sources available. One natural medicinal plant known to possess pharmacological activity and offer numerous benefits as a medicinal plant is the bajakah plant (*Spatholobus littoralis* Hassk).(7) In addition, bajakah stems are proven to contain phenolic secondary metabolite compounds, flavonoids, tannins, and saponins, which, according to some previous studies, have been shown to have antidiabetic, strong antioxidant, and anti-inflammatory effects.(8,9)

Secondary metabolite compounds from natural materials that are reported to have activity as anti-hyperuricemia are flavonoids, alkaloids, and tannins, where flavonoids work by inhibiting xanthine oxidase so as to reduce excessive uric acid production, alkaloids are also able to suppress and reduce the frequency of acute attacks and relieve pain by inhibiting the synthesis and release of leukotrienes. While tannin compounds are known to bind free radicals during the change of purines into uric acid, tannins have astringent effectiveness so that they can shrink mucous membranes.(10) Bajakah plants are reported to contain several secondary metabolite compounds, such as steroids, that can act as anti-inflammatory,(8) flavonoids have anti-inflammatory potential by inhibiting COX-2 and lipooxygenase enzymes.(11,12)

The various research reports have revealed the diverse bioactive compounds present in bajakah and its strong antioxidant effects; however, the potential of bajakah as an anti-hyperuricaemic agent in cases accompanied by inflammation has not yet been fully explored. Consequently, this study was conducted with the aim of investigating the role of bajakah stem extract as an anti-hyperuricaemic agent, based on the reduction in uric acid levels and the inhibition of cyclooxygenase-2 in an animal model of hyperuricemia.

METHODS

The research began with the collection and preparation of samples, then the maceration method extraction was carried out by soaking 1 kg of bajakah stem powder into a macerator container using 96% ethanol solvent as much as 2.5 liters for 3 x 24 hours. The filtrate is collected and concentrated by rotating evaporation using a rotary vacuum evaporator at 50°C until a thick extract is obtained. Furthermore, acclimatization of test animals was carried out to observe the behavior and adaptability of test animals and prevent stress in their new environment in the research room for ± 1 week at room temperature.(13,14,15)

The treatment of test animals involved 24 mice based on Federer's formula; they were fasted for 10 hours and then randomized into 6 groups of test animals consisting of normal groups, negative controls, positive controls, and variations in extract doses. Then the blood was taken through the lateral vein of the mice's tail to measure the initial uric acid level. Then induced with 0.2 mL potassium oxonate solution intraperitonially in addition to the normal group and left for 1 hour for modeling hyperuricemia mice. Furthermore, the division of treatment groups was carried out and given treatment via the oral route, namely: a normal group is a group of mice without treatment; negative control is given 0.5% Na-CMC treatment; positive control is given allopurinol suspension at a dose of 0.0018 mg/kg BW; extract group doses of 100, 200 and 300 mg/kg BW. Uric acid levels were measured again after treatment at the 1st hour (t60), 2nd (t120), and 3rd (t180) using the lateral chromatography method, where the test stick has a part that can absorb whole blood from the location of the blood drop into the reaction zone. Uric oxidase in the reaction zone then oxidizes uric acid in the blood and the intensity of the electron current is measured by the device and read as the concentration of uric acid in the blood sample in mg/dL. After that, the animals were dissected, and blood was taken from the mice through the heart using a spoit, then put into an EDTA tube and centrifuged to get a plasma sample. The plasma was obtained into an eppendorf tube and then tested for COX-2 levels using the ELISA method by following the steps in the kit procedure.(16,17) The data were analyzed with one-way ANOVA and LSD post-hoc tests, and a correlation test. This study has received ethical clearance from the Health Research Ethics Committee of the UHO LPPM (National Institute of Health Research) under the number: 183a/UN29.20.1.2/PG/2023.

RESULT

Animal Modeling of Hyperuricemia

Mice acclimatized for 7 days were examined for initial uric acid levels to confirm within the normal range of 1.7 - 3.0 mg/dL; then hyperuricemia was induced by 250 mg/kg BW of potassium oxonate via intraperitoneal injection to achieve hyperuricemia more rapidly. This condition was confirmed based on measurements of uric acid levels in the mice before and after potassium oxonate induction, as shown in Figure 1.

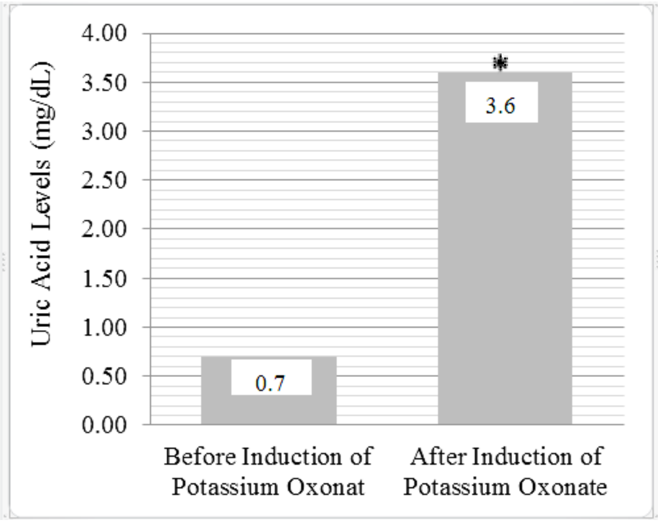

Figure 1. Measurement of mean uric acid levels before and after potassium oxonate induction. (Note: paired t-test analysis * = p<0.05 significantly different)

The average results of uric acid levels before and after potassium oxonate induction in Figure 1 show an increase in uric acid levels after potassium oxonate induction from the initial uric acid level of 0.70 mg/dL increased to 3.6 mg/dL. These results indicate that potassium oxonate can increase the uric acid levels of mice beyond the range of normal levels so that hyperuricemia modeling of test animals can be done in this study.

Measurement of Uric Acid Level in Animals Test

The results of the study measuring blood uric acid levels at the 1st, 2nd, and 3rd hours after treatment showed a decrease in uric acid levels in the positive control group and the three extract dose variations, while the negative control group showed an increase in uric acid levels. The average uric acid levels in each group after treatment are shown in Table 1.

The results in Table 1 show that all treatment groups receiving extract doses had a significantly different effect compared to the negative control in reducing uric acid levels from 60 to 180 minutes (p<0.05), and were not significantly different from the positive control at doses of 200 and 300 mg/kg BW at 60 and 120 minutes (p>0.05), while the 100 mg/kg BW dose did not differ significantly at 180 minutes (p>0.05).

Table 1. Uric Acid Level of Each Group after Treatment

Group	Replication (N)	Average Difference in Reduction of Uric Acid Levels (mg/dL) ± SD (mg/dl)		
		1st hour (T60)	2nd hour (T120)	3rd hour (T180)
Normal control	4	0.70±0.18	0.70±0.24	0.69±0.12
Negative control	4	4.60±0.49	4.90±0.48	5.28±0.70
Positive control	4	4.13±0.37	3.70±0.41*[a]	2.58±0.20*[a]
Dose 100 mg/kg BW	4	3.78±0.68*[ab]	3.60±0.63*[a]	3.33±0.62*[ab]
Dose 200 mg/kg BW	4	3.35±0.31*[ab]	3.13±0.34*[ab]	2.80±0.34*[a]
Dose 300 mg/kg BW	4	3.53±0.35*[ab]	3.25±0.36*[ab]	2.33±0.35*[a]

Note: significantly different ($p<0.05$); a = significantly different from negative control; b = significantly different from positive control.

To determine the best effect of reducing uric acid levels in each group, the average difference in uric acid levels in test animals was calculated. The average difference in the decrease in uric acid levels after treatment for each group is shown in Table 2.

Table 2. Average Difference in Reduction of Uric Acid Levels in Animals Test

Group	Average Difference in Reduction of Uric Acid Levels (mg/dL) ± SD		
	1st hour (T60)	2nd hour (T120)	3rd hour (T180)
Normal control	0	0	0
Negative control	-0.35±0.17	-0.30±0.08	-0.38±0.23
Positive control	1.38±0.38*[a]	0.43±0.05*[a]	1.13±0.32*[a]
Dose 100 mg/kg BW	0.13±0.05*[b]	0.18±0.03*[b]	0.28±0.09*[b]
Dose 200 mg/kg BW	0.18±0.04*[b]	0.23±0.05*[b]	0.33±0.07*[b]
Dose 300 mg/kg BW	0.35±0.03*[b]	0.28±0.06*[b]	0.33±0.06*[b]

Note: significantly different ($p<0.05$); a = significantly different from negative control; b = significantly different from positive control.

Based on the difference in the decrease in uric acid levels in Table 2, it shows that the effect of reducing uric acid levels is best in the positive control group and the treatment of extracts of the three-dose variations, based on the magnitude of the difference in reducing uric acid levels at hours 1 to 3.

Measurement of COX-2 Level

COX-2 inhibition testing using ELISA method with prostaglandin endoperoxide synthase-2 (PTGS2/COX-2) Kit. The selection of the Sandwich ELISA method is because this type of ELISA has high specificity so it is expected to be able to show accurate results on the test sample. The results of the average measurement of COX-2 levels after treatment of test animals in this study can be seen in Figure 3.

The results of measuring COX-2 levels after extract treatment showed the highest COX-2 levels in the negative control (3.9 ng/mL), 100 mg/kg BW dose extract (3.1 ng/mL), 200 mg/kg BW dose extract (2.21 ng/mL), and the lowest COX-2 levels in the 300 mg/kg BW dose extract group (1.1 ng/mL) which were the same as the levels in the normal group (1.1 ng/mL) and positive control (1.4 ng/mL).

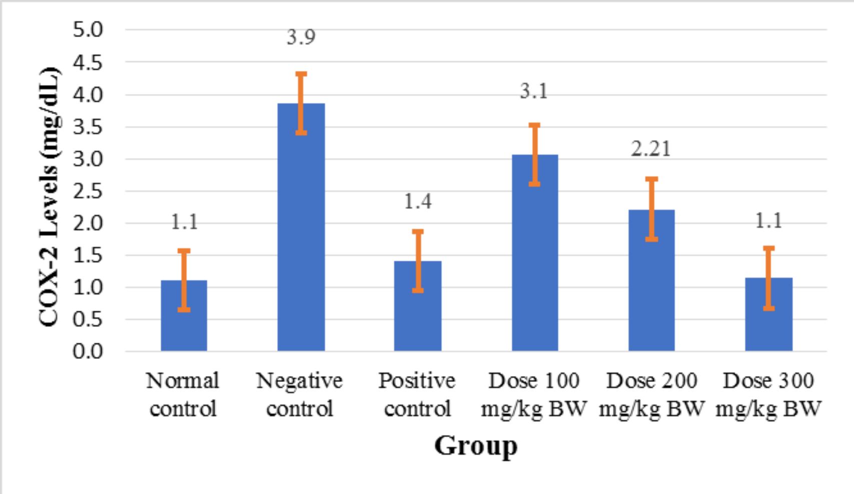

Figure 3. Average COX-2 Level after Treatment

DISCUSSIONS

Effects of lowering Uric Acid Levels

Antihyperuricemia activity testing in this study aims to determine the ability of Bajakah stem ethanol extract to reduce uric acid levels and inhibit COX-2 formation in test animals that experience hyperuricemia, and reveal whether there is a correlation between uric acid levels and COX-2 levels carried out in vivo. Previous research explained that uric acid is thought to play a role in modulating cyclooxygenase-2 levels in the body by activating the proliferation pathway in vascular smooth muscle cells (VSMC), and uric acid augmentation of VSMC proliferation in the renal artery is mediated by COX-2, so studying the relationship between the two parameters is needed.(3) Likewise, the results of other studies explain that the effects of uric acid increase COX-2 concentrations significantly and are directly related to inflammatory mediators, prostaglandins, and VSMC proliferation.(18)

Based on the results of the research conducted, it was found that there was a decrease in uric acid levels in test animals that experienced hyperuricemia after being given the bajakah stem extract, which differed significantly from the negative control group Na.CMC ($p<0.05$). This shows that the administration of Bajakah stem extract of all dose variations has the effect of reducing uric acid levels. Na.CMC in this study serves as a carrier agent in extracts and positive controls, and has no pharmacological effect or effect on reducing blood uric acid levels in animal tests(19). The positive control (allopurinol) showed a decrease in uric acid levels comparable to that in the extract group, with a p-value of>0.05. Allopurinol is an anti-hyperuricemia drug of first choice therapy with a mechanism of action that inhibits xanthine oxidase and affects the inhibition of purine formation into uric acid so that urate crystal formation does not occur and inhibits purine synthesis as a precursor to xanthine.(20,21)

The effect of reducing uric acid levels based on the magnitude of the difference in the decrease in mice blood uric acid levels was shown by the three variations of extract doses, although it was not comparable to the magnitude of the difference in the decrease in uric acid levels in the positive control group at the 1st hour to the 3rd hour (Table 2), statistically, there was no significant difference in the dose of extract treatment group with positive control ($p<0.05$). This shows that the administration of Bajakah stem extract is able to reduce uric acid levels in hyperuricemic mice.

Preliminary research has reported that ethanol extracts of bajakah stems contain secondary metabolites, including alkaloids, flavonoids, phenolics, and tannins.(22,8) It has been reported that, among these secondary metabolites, flavonoids play a role in lowering uric acid levels by preventing the formation of free radicals through the suppression of ROS and by inhibiting the activity of the xanthine oxidase enzyme(6,22). Previous studies have also shown that flavonoid compounds have xanthine oxidase inhibitory activity in vivo and can reduce COX-2 excretion in mice, which has potential as an antioxidant and anti-inflammatory.(23,24)

Effects of COX-2 Inhibition

The COX-2 inhibitory effect in test animals after bajakah stem extract treatment is indicated by a decrease in COX-2 levels compared with the negative control group (na. CMC) in hyperuricemic mice, with COX-2 levels remaining high and directly proportional to high uric acid levels. Based on the results of the post hoc LSD statistical test of COX-2 data, it shows that between the negative control and the extract dose variation group, there is a significant difference ($p<0.05$) between the negative control and the extract dose variation group, which means that the extract dose variation group has the potential to inhibit the formation of COX-2 in test animals that experience hyperuricemia. While the positive control (allopurinol) showed COX-2 levels significantly different ($p<0.05$) from the extract dose groups of 100 and 200 mg/kg BW, where COX-2 levels in the positive control were lower than the treatment of the two dose variations, which means that the positive control COX-2 inhibition is better than the two variations of the extract dose. Whereas between the positive control and the 300 mg/kg BW dose of extract treatment, there was no significant difference ($p>0.05$) in COX-2 levels after treatment, which means that the COX-2 inhibitory effect of the 300 mg/kg BW dose of extract is the same as the positive control, so it can be assumed that the 300 mg/kg BW dose of extract treatment effectively inhibits COX-2 in hyperuricemia conditions.

The COX-2 inhibitory effect on bajakah stem samples is influenced by the content of secondary metabolite compounds. It is known that bajakah stems contain compounds that are thought to act as COX-2 inhibitors, including alkaloids, flavonoids, steroids, terpenoids, saponins, tannins, and phenols which are thought to play a role in COX-2 inhibition, and purine synthesis. These compounds have been known to have anti-inflammatory effects and also have the effect of reducing uric acid levels that work as cyclooxygenase (COX) inhibitors that function to trigger the formation of prostaglandins. (25,26)

According to previous research, flavonoid compounds in bajakah can act as anti-inflammatories. The mechanism of action of flavonoids as anti-inflammatories is by inhibiting the enzyme cyclooxygenase-2 during the inflammatory process.(8) Flavonoid compounds, especially quercetin, are thought to suppress COX-2 expression in test animals. This is in line with previous research where the flavonoid compound quercetin, as a COX-2 inhibitor using the molecular docking computational approach method, shows that the results of flavonoid compounds (quercetin) have the best free bond energy, so that they have strong COX-2 inhibitor potential.(10,27)

Relationship of Uric Acid Level with COX-2

The correlation testing of uric acid levels with COX-2 levels was conducted to determine whether there is a relationship between increased uric acid levels and increased COX-2 levels, or vice versa, in the test animals. The basis for interpreting these test results is that a significance value <0.05 indicates a significant correlation, whereas a significance value >0.05 indicates that there is no correlation between the variables. Based on the results of the correlation test, a correlation between uric acid levels and COX-2 was found with a p-value of 0.000, meaning the correlation between uric acid levels and COX-2 is significant (p<0.05). The correlation coefficient was 0.704, indicating a strong correlation. Furthermore, the correlation coefficient is positive, indicating that the relationship between uric acid levels and COX-2 is direct; that is, a decrease in uric acid levels is directly proportional to a decrease in COX-2 levels, and conversely.

The findings of this study indicate that there is a correlation between uric acid levels and COX-2 expression. This is due to uric acid's role in modulating COX-2 expression in the body by activating the proliferation pathway in vascular smooth muscle cells (VSMC), and to uric acid's augmentation of VSMC proliferation in renal arteries, mediated by COX-2.(3) Other studies show that measuring uric acid levels in hyperuricemia conditions directly increases COX-2 concentrations, which are influenced by the VSMC synthesis pathway.(7) The findings of this study are also supported by research conducted by Sumarya (2021), explaining that uric acid induces an inflammatory response of VSMC proliferation and endothelial cell dysfunction by activating the immune system and changing the characteristics of VSMC and endothelial cells, through the formation of ROS and COX-2(28). This study can reveal the role of the bajakah stem extract in reducing uric acid levels and, at the same time, inhibiting COX-2 expression as an inflammatory mediator, suggesting its potential to be further developed as an anti-hyperuricemia and anti-inflammatory agent for the treatment of gout or rheumatoid arthritis.

CONCLUSION AND RECOMMENDATIONS

Ethanol extract of bajakah stem has anti-hyperuricemia activity by reducing uric acid levels and is positively correlated with inhibition of COX-2 expression in hyperuricemia test animals. Results of this study suggest that bajakah stems have the potential to be further developed as an herbal drug with antihyperuricemic and anti-inflammatory properties.

ACKNOWLEDGMENTS:

The authors thank the Pharmacy Research Laboratory of the Faculty of Pharmacy and the Laboratory of the Faculty of Medicine, University of Halu Oleo, who have facilitated the implementation of this research.

REFERENCES

1. Arjani IAMS, Mastra N, IWayan M. Overview of Uric Acid Levels and Knowledge Levels of the Elderly in Samsam Village, Kerambitan District, Tabanan Regency. Meditory (The J Med Lab. 2018;6(6):46–55.
2. Feng S, Wu S, Xie F, Yang CS, Shao P., Sijie Wu. Trends Food Sci Technol. 2022;123(May 2022):87–102.
3. Kirca M, Uzuner F. Uric acid stimulates proliferative pathways in vascular smooth muscle cells through the activation of p38 MAPK , p44 / 42 MAPK and PDGFR β. J Recept Signal Transduct Res 3. 2017;37(2):1–7.
4. Xuan Y, Guo Y, Zhu Y, Wang O, Rokosh G, Messing RO, et al. Signaling Cascade in the Activation of Signal Transducers and Activators of Transcription 1 and 3 and Induction of Cyclooxygenase-2 After Ischemic Preconditioning. Circulation. 2005;112(13):1971–8.
5. Russo E, Bertolotto M, Zanetti V, Picciotto D, Esposito P, Carbone F, Montecucco F, Pontremoli R, Garibotto G, Viazzi F, Verzola D. Role of Uric Acid in Vascular Remodeling: Cytoskeleton Changes and Migration in VSMCs. Int J Mol Sci. 2023 Feb 3;24(3):2960.
6. Asriullah Jabbar, Halik, Fadhliyah Malik, Muhammad Ilyas Y, Jamal Qadar, Hasyrul Hamzah, Sylvia Utami Tunjung Pratiwi. Antihyperurisemia Activity of Etanol Extract of *Etlingera rubroloba* A.D Poulsen Fruits on Uric Acid and Cyclooxygenase-2 Levels In Vivo. Res J Pharm Technol.2024; 17(4):1627-1.
7. Ayuchecaria N, Saputera MMA, Niah R. Determination of Total Phenolic Content of Bajakah Tampala (*Spatholobus littoralis* Hassk.) Stem Extract Using UV-Visible Spectrophotometry. J Insa Farm Indones. 2020;3(1):132–41.
8. Nastiti K, Nugraha DF. Anti-inflammatory Activity of Bajakah Wood Extract (*Spatholobus littoralis* Hask). Jurnal Surya Medika (JSM). 2022 Feb 1;7(2):45-50.
9. Amiani W, Fahrizal MR, Aprelea RN. Secondary metabolite content and activity of bajakah plant as antioxidant agent. J Health Sains. 2022 Apr 26;3(4):516-22.
10. Rakanita Y, Hastuti, Tandi J, Mulyani S. Antihyperuricemia Effectiveness of Celery Leaf Ethanol Extract (Eeds) in Potassium Oxonate Induced Rats. Trop Pharm Chem. 2017;4(1):1–6.
11. Susanto BN, Marsepa E. Anti-inflammatory and Antipyretic Effects of Bajakah Tampala Stem Extract (*Spatholobus littoralis* Hassk) on Mice (*Mus musculus* L.). Jurnal Ilmiah Biosaintropis (Bioscience-Tropic). 2022 Aug 10;8(1):33-45.
12. Yusuf MI, Wahyuni, Susanty S, Ruslan, Fawwaz M. Antioxidant and antidiabetic potential of galing stem extract (*Cayratia trifolia* Domin). Pharmacogn J. 2018;10(4).
13. Yusuf MI, Firdayanti, Wahyuni. Enhancement Of Non Specific Immunity (Innate Immunity) Mice Balb/C Given Ethanol Extract Of Galing Plant (*Cayratia trifolia* L). Med Sains. 2019;3(2):83–92.
14. Jabbar A, Sahidin I, Monstavevi SA, Malaka MH, Malik F, Ilyas YM. Antioxidant and Anti-Inflammatory Activity of Ethanol Extract Stem of *Etlingera rubroloba* A.D. Poulsen. Pakistan J Biol Sci. 2022;25(10):885–91.
15. Y MI, Saehu MS, Ertin, Irma, Nurhikma. Anti-inflammatory Effect of Fractions from Ethanol Extract of Galing Stem (*Cayratia trifolia* L.Domin) In Vitro (Efek Antiinflamasi Fraksi Dari Ekstrak Etanol Batang Galing (*Cayratia trifolia* L.Domin) Secara In Vitro. J Farm Sains dan Prakt. 2021;(Desember):80–8.
16. Jabbar A, Wahyuni, Leorita M, Yusuf MI, Salsabila H, Sahidin I. Antihyperuricemia Activity Of Wualae Fruit (*Etlingera elatior* Jack R.M.Smith) Ethanol Extract In Vivo. J Farm Sains dan Prakt. 2021;7(3):313–20.
17. Daud, Nur Saadah, et al. Antihyperuricemia Activity of Ethanol Extract of Galing Leaf (*Cayratia trifolia* L. Domin) in BALB/C Mice. Warta Farmasi, 2019; 8(2): 20-30.
18. Oguz N, Kırça M, Çetin A, Yeşilkaya A. Effect of uric acid on inflammatory COX-2 and ROS pathways in vascular smooth muscle cells. J Recept Signal Transduct. 2017;37(5):500–505.
19. Mahmudah R, Yusuf MI, Ode W, Nur I, Bina P, Kendari H. Antihyperuricemia Effectiveness Test of Combination of Ethanol Extract of Moringa Leaves (*Moringa aloeifere* L.) and Sukun Leaves (*Artocarpus altilis*) in Male Rats (*Rattus norvegicus*). J Mandala Pharmacon Indones. 2023;9(2):532–42.
20. Brucato A, Cianci F, Carnovale C. European Journal of Internal Medicine Management of

hyperuricemia in asymptomatic patients : A critical appraisal. Eur J Intern Med. 2020;74(April 2019):8–17.

21. Winder M, Owczarek AJ, Mossakowska M, Broczek K, Grodzicki T, Wierucki Ł, Chudek J. Prevalence of Hyperuricemia and the Use of Allopurinol in Older Poles-Results from a Population-Based PolSenior Study. Int J Environ Res Public Health. 2021 Jan 6;18(2):387.
22. Azzahra A, Farhani N, Syahfitri W, Pasaribu SF. Potential Flavonoid Content in Bajakah Wood as Antidiabetic. Jurnal Pendidikan Tambusai. 2022 Jul 16;6(2):14345-50.
23. Ilyas MY, Sahidin I, Jabbar A, Yodha AWM, Diantini A, Pradipta IS, et al. Effect of Immunomodulating Extract and Some Isolates from *Etlingera rubroloba* A.D. Poulsen Fruits on Diabetic Patients with Tuberculosis. Molecules. 2023;28(5):1–15.
24. Ifora I, Sintia B dan Srangenge Y. Effect of Cyclooxygenase-2 Enzyme Inhibition and Anti-inflammatory Activity of Coriander Leaf Extract (*Coriandrum sativum* L.) Jurnal Kefarmasian Indonesia. 2021: 11(1), 17–24.
25. Wang T yang, Li Q, Bi K shun. Bioactive flavonoids in medicinal plants: Structure, activity and biological fate. Asian J Pharm Sci. 2018 Jan 1;13(1):12–23.
26. Wang, Q., Jin, J., Dai, N., Han, N., Han, J., & Bao, B. Anti-inflammatory effects, nuclear magnetic resonance identification, and high-performance liquid chromatography isolation of the total flavonoids from Artemisia frigida. Journal of food and drug analysis. 2016: 24(2), 385–391.
27. Ahsana D, Andika A dan Nashihah S. Molecular Docking Study Of Flavonoid Compounds In The Guava Leaves (*Psidium guajava* L.) Which Has Potential As Anti-Inflammatory COX-2 Inhibitors. Lumbung Farmasi: Jurnal Ilmu Kefarmasian. 2021: 2(2).
28. Sumarya IM, Suanda IW. Uric Acid Induces Inflammatory Response VSCM Proliferation and Endothelial Cell Dysfunction. Widya Biol. 2021;12(1):48–57.