17% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

Filtered from the Report

- Bibliography
- Cited Text

Match Groups

30 Not Cited or Quoted 17%
Matches with neither in-text citation nor quotation marks

0 Missing Quotations 0%
Matches that are still very similar to source material

0 Missing Citation 0%
Matches that have quotation marks, but no in-text citation

0 Cited and Quoted 0%
Matches with in-text citation present, but no quotation marks

Top Sources

17% Internet sources
13% Publications
5% Submitted works (Student Papers)

Integrity Flags

0 Integrity Flags for Review

No suspicious text manipulations found.

Our system's algorithms look deeply at a document for any inconsistencies that would set it apart from a normal submission. If we notice something strange, we flag it for you to review.

A Flag is not necessarily an indicator of a problem. However, we'd recommend you focus your attention there for further review.

Match Groups

- **30** Not Cited or Quoted 17%
  Matches with neither in-text citation nor quotation marks
- **0** Missing Quotations 0%
  Matches that are still very similar to source material
- **0** Missing Citation 0%
  Matches that have quotation marks, but no in-text citation
- **0** Cited and Quoted 0%
  Matches with in-text citation present, but no quotation marks

Top Sources

17% Internet sources
13% Publications
5% Submitted works (Student Papers)

Top Sources

The sources with the highest number of matches within the submission. Overlapping sources will not be displayed.

1	Internet	www.ncbi.nlm.nih.gov 2%
2	Internet	repositori.usu.ac.id 1%
3	Publication	Endang Nurcahyani, Novita Herliani, M Kanedi M Kanedi. "Antihyperuricemia Acti... 1%
4	Internet	repository.lppm.unila.ac.id 1%
5	Student papers	Universitas Airlangga <1%
6	Internet	elearning.medistra.ac.id <1%
7	Student papers	October University for Modern Sciences and Arts (MSA) <1%
8	Internet	journal2.unusa.ac.id <1%
9	Internet	topsecretapiaccess.dovepress.com <1%
10	Publication	van Raaij, J. M. A.. "Influence of Human Diets Containing Casein, Soy Protein Isola... <1%

11	Internet	
earthpressnews.com		<1%
12	Internet	
pdffox.com		<1%
13	Internet	
repository.unimus.ac.id		<1%
14	Internet	
www.rjpbcs.com		<1%
15	Internet	
www.researchgate.net		<1%
16	Internet	
journals.lww.com		<1%
17	Internet	
fkp.utem.edu.my		<1%
18	Internet	
garuda.kemdikbud.go.id		<1%
19	Internet	
nnpub.org		<1%
20	Internet	
phcogj.com		<1%
21	Internet	
www.coursehero.com		<1%

EFFECTIVENESS TEST OF BAY LEAF ETHANOL EXTRACT AS ANTIHYPERURICEMIA INVIVO

Hilda S[1] , Rosnike Merly Panjaitan[1], Nurul Hidayah[1*]

[1]Diploma III Pharmacy Study Program, Department of Pharmacy, Health Polytechnic, Ministry of Health of the Republic of Indonesia, Medan

Email corespondensi : nurul.hidayah3607@gmail.com

Track Record Article

Accepted:

Published:

Abstract

The imbalance between high production and low excretion of uric acid in the body causes hyperuricemia which then has the potential to cause gout. This disease is the second largest after stroke in Indonesia. Conventional therapy is not free from adverse effects. The tendency of society to go back to nature and the government's "Saintifikasi Jamu" program are efforts to explore safer alternative therapies. One of the plants that has the potential as an antihyperuricemia is bay leaves (Syzygium polyanthum Walp.). The purpose of this study is to optimize the use of scientifically based bay leaves as an antihyperuricemia agent. The research method used is experimental with a pre-posttest design . A total of 20 mice were divided into 5 test groups (induction, comparison, bay leaf extract group (EEDS) with doses of 100 mg/kgBW, 200 mg/kgBW and 400 mg/kgBW. The effectiveness of antihyperuricemia was tested by inducing mice with 1% chicken liver juice and potassium oxonate. Uric acid levels were measured at T1, T7 and T14 days of the study using a Blood Uric Acid Meter. All groups of test extract doses showed effectiveness as agents to lower uric acid levels significantly compared to the induction group ($p<0.05$). The potential effectiveness of antihyperuricemia extract showed an effect that was not statistically different from the comparison (allopurinol) ($p>0.05$) at all measurement points. The conclusion of this study shows that bay leaf ethanol extract has the potential as an antihyperuricemia agent where a dose of 100 mg/kgBW showed the best effectiveness as an antihyperuricemia

Keyword: Bay leaves, Extract, chicken liver, Potassium oxonate, Uric acid

INTRODUCTION

Uric acid is the end result of purine catabolism. Uric acid is a waste product of this purine. Purine is a natural substance that is one of the chemical structure groups that form DNA and RNA. For normal uric acid levels in men range from 3.5-7 mg/dL and in women 2.6-6 mg/dL (RI, 2019) . If uric acid production increases or the kidneys are unable to remove uric acid from the body and both, then uric acid levels in the blood will increase. This condition is called hyperuricemia (Papadakis & Mcphee, 2019) . Hyperuricemia is a condition in which there is an increase in uric acid levels (up to above 7.0 mg/dL for men and 6.0 mg/dL for women) in the body. Gout, also known as gout, is a disease caused by the accumulation of monosodium urate crystals in the body, causing joint pain (gouty arthritis), lumps in certain parts of the body (tophi), and disorders and stones in the urinary tract (Dira et al., 2015) . Increased serum uric acid levels known as hyperuricemia are considered to be one of the factors in the progression of kidney disorders and chronic kidney disease (Wariki Maria C; Ealeleng,

BJ; Pandelaki, 2022) . The incidence of gouty arthritis in recent decades in both developed and developing countries has increased, especially in men aged 40-50 years. The prevalence of hyperuricemia is approximately 2.6 - 47.2% which varies in various populations. While the prevalence of gout varies between 1 - 15.3% (RI, 2019; Singh & Gaffo, 2020) .

There are two groups of hyperuricemia drugs, namely drugs that stop the acute inflammatory process (colchicine, indomethacin) and drugs that affect uric acid levels (probenecid, allopurinol). For acute conditions, NSAID drugs can be used. Common side effects of allopurinol are allergic reactions, digestive disorders, leukopenia, arthralgia, and pruritus (Department of Pharmacology and Therapeutics, 2016) . Therefore, it is necessary to explore alternative therapies that are relatively safer. The tendency of society to go back to nature and the government policy that has launched the "Jamu Saintification" program with a priority on preventive research on 4 formula herbs (hyperglycemia, hypertension, hyperolesterolemia, and hyperuricemia) are prospective conditions for developing research on plants based on Indonesian biodiversity (Muammar, 2014) . One of the plants that has the potential as an antihyperuricemia is bay leaves (Syzygium polyanthum Walp).

Previous studies of several plants showed that bay leaf water extract at a dose of 200 mg/kgBW of mice showed the greatest antihyperuricemia ability (79.35%) compared to other plants (Darussalam & Rukmi, 2019; Hidayah et al., 2018; Ningtiyas & Ramadhian, 2016; Yanti et al., 2021) . Bay leaves contain flavonoids and tannins which are thought to be responsible for inhibiting the action of xanthine oxidase and superoxidase, thereby reducing uric acid levels in the blood, and inhibiting the action of the cyclooxygenase enzyme, thus showing anti-inflammatory effects (Hidayah et al., 2018; Hidayat & Wulandari, 2021; Muammar, 2014; Nadhifah & Hidayati, N; Suhendy, 2021; Nur & Sumiwi, 2020; Somalinggi et al., 2023) . Based on the above explanation, a study was conducted on the effectiveness of ethanol extract of bay leaves as an antihyperuricemia using 1% chicken liver juice and potassium oxonate as induction.

METHODS

Tools and materials

The tools used are maceration tool, rotary evaporator, water bath, 1 ml syringe, 5 ml syringe, oral sonde, animal scales, analytical scales, animal cages, cotton, measuring cups, dropper pipettes, mortars, stampers, spatulas, Blood Uric Acid Meter measuring tools, uric acid strips.

The materials used in this study were bay leaves, CMC Na, allopurinol, distilled water, 96% ethanol, flannel cloth, filter paper, potassium oxonate, chicken liver juice, healthy male mice weighing 20-30 g, aged 2-3 months.

Preparation of Simplisia and Extract

As much as 2 kg of fresh bay leaves are washed, drained, dried and then powdered. The powdered simplicia is macerated with 70% ethanol. The extraction results are then filtered and concentrated using a rotary evaporator and evaporated on a water bath until a constant weight is obtained.

Determination and Characterization of Simple Ingredients

Bay leaf simplicia was determined at the Medanese Herbarium of the University of North Sumatra (USU). Characterization of simplicia and extracts carried out included testing water content, ash content, ethanol-soluble extract content, water-soluble extract content, and specific gravity. Characterization was continued with phytochemical screening of the extract including examination of alkaloids, saponins, quinones, tannins, saponins, flavonoids, and steroids/triterpenoids and TLC testing.

Testing Activity Antihyperuricemia

The method of testing antihyperuricemic activity is carried out based on a modification of the method used. (Assegaf, 2019; Guidance et et al., 2018). Each group test animal consists of on 5 tail mice.

Distribution group animal test among others:

Group normal, group comparator (allopurinol 10mg/kgBW), group induction (juice chicken liver 0.2% b/v And potassium oxonate ip dose 250 mg/kg BB), And group extract (dose 50 mg/kgBW; 100 mg/kgBW, and 200 mg/kgBW).

Induction condition hyperuricemia done with method give juice chicken liver 0.2% w/v daily for 14 days and administration of potassium oxonate ip at a dose of 250 mg/kg BW 1 hour before administration of the test extract.

Determination level sour tendon blood mice are done on day to- 1, 7, And 14 day. After it is done measurement on time beginning (t0), furthermore given juice heart chicken 0.2% b/v and potassium oxonate 250 mg/kg BW. After 1 hour, the carrier preparation, comparator and test extract were given. Examination level sour tendon blood furthermore done on minute 60th And 120th after administration of the test preparation.

Blood uric acid levels are measured using a test strip that has been installed on Easy Touch®, Where level sour tendon blood will readable in time 10 seconds.

Statistical Analysis

The research data were analyzed univariately (mean data (mean) of uric acid levels and standard deviation per group of test animals) which were presented in the form of tables and graphs. While bivariate analysis was carried out using ANOVA and continued with the Tukey post hoc test with a confidence level of 95%.

RESULTS

Uric acid level measurements were carried out on days 1, 7, and 14. Each time the blood uric acid level was measured was carried out 3 times (T0, T1, and T2). The determination of the optimal blood collection time in this study refers to previous studies that obtained the results that optimal blood collection occurs at 1 hour after induction with potassium oxonate (Ariyanti et al., 2007) . The longer the blood collection time after induction with potassium oxonate, the lower the uric acid level in the blood. This is likely due to the short half-life of potassium oxonate or the elimination process from the body that is too fast so that the potassium oxonate in the blood has run out, which causes potassium oxonate to be unable to inhibit uricase in the process of breaking down uric acid into allantoin (Ariyanti et al., 2007) . Based on this, it was determined that the observation of uric acid level measurements was carried out up to 2 hours after induction.

Table 1. Uric acid levels on day 1 of the study (T1)

Test Group	Uric Acid Level (T1)		
	T0	T1	T2
Induction	3.73 ± 0.41	5.03 ± 1.49	7.15 ± 0.74
Comparator	7.50 ± 2.84	4.45 ± 0.70	4.30 ± 0.67
EEDS 400 mg/kg BW	5.35 ± 0.82	4.58 ± 1.06	3.65 ± 1.30
EEDS 200 mg/kg BW	9.30 ± 4.22	8.43 ± 3.78	5.00 ± 1.02
EEDS 100 mg/kg BW	6.73 ± 2.65	5.35 ± 1.65	4.60 ± 1.58

Table 2. Uric acid levels on the 7th day of the study (T7)

Test Group	Uric Acid Levels (T7)		
	T0	T1	T2
Induction	7.08 ± 4.20	8.40 ± 4.20	10.05 ± 3.45
Comparator	6.58 ± 2.40	3.98 ± 0.71	3.35 ± 0.41
EEDS 400 mg/kg BW	9.05 ± 2.92	7.73 ± 2.85	5.63 ± 2.20
EEDS 200 mg/kg BW	5.03 ± 1.29	4.98 ± 0.62	4.25 ± 0.74
EEDS 100 mg/kg BW	11.25 ± 6.72	5.63 ± 2.96	5.33 ± 2.46

Table 3. Uric acid levels on the 14th day of the study (T14)

Test Group	Uric Acid Level (T14)		
	T0	T1	T2
Induction	9.98 ± 2.10	11.58 ± 2.67	15.90 ± 1.91
Comparator	5.15 ± 0.59	3.93 ± 0.90	3.13 ± 0.15
EEDS 400 mg/kg BW	7.53 ± 0.90	6.08 ± 0.88	4.73 ± 1.41
EEDS 200 mg/kg BW	6.10 ± 1.16	5.50 ± 1.28	4.50 ± 1.37
EEDS 100 mg/kg BW	7.13 ± 1.63	5.73 ± 0.96	4.23 ± 1.04

Information :

T0 = time for measuring uric acid levels 1 hour after administration of potassium oxonate and 1% chicken liver juice

T1 = time of measurement of uric acid levels 1 hour after oral administration of the test preparation

T2 = time of measurement of uric acid levels 2 hours after oral administration of the test preparation

Based on Tables 1, 2 and 3, the results showed that after 1 hour of administration of 1% b/v chicken liver and 250 mg/kgBW potassium oxonate, there was an increase in blood uric acid levels in test animals from normal conditions (before induction). This shows that the inducer used was successful in inhibiting the uricase enzyme, thereby inhibiting the conversion of uric acid to allantoin, so that blood uric acid levels increased. All EEDS and comparison groups (allopurinol) showed effectiveness in reducing blood uric acid levels in test animals. These results are in accordance with previous studies which stated that bay leaf extract has the potential as an antihyperuricemia (Hidayah et al., 2018) . Hyperuricemia conditions in test animals were carried out by giving 1% b/v chicken liver juice and 250 mg/kgBW potassium oxonate. Chicken liver is used because it contains high levels of purine as a raw material for forming uric acid, while potassium oxonate works by inhibiting the uricase enzyme which converts xanthine into allantoin so that blood uric acid levels increase (Saharuddin, M; Titawanno, 2019) .

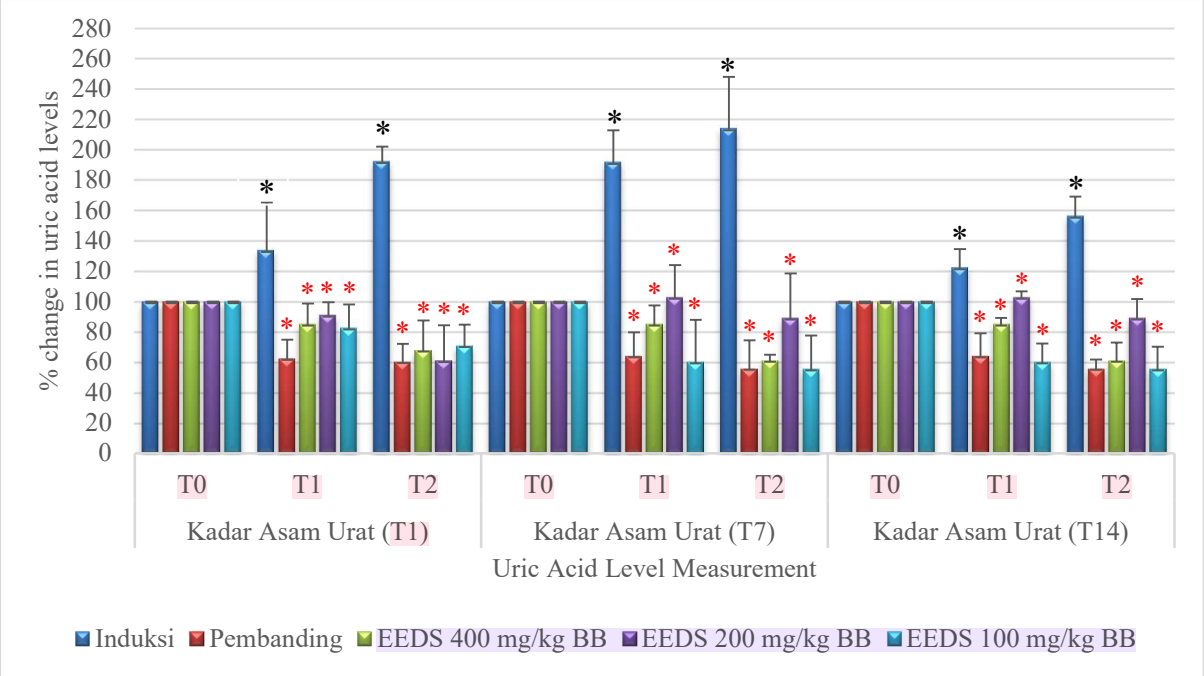

Figure 1. Graph of percentage changes in blood uric acid levels in test animals

Information:
* = ($p<0.05$) compared to induction group
* = ($p<0.05$) compared to comparison group

Based on Figure 1 above, hyperuricemia measurements at T1 and T2 showed that all EEDS dose groups and the comparison group had shown a significant decrease in blood uric acid levels compared to the induction group ($p <0.05$) starting from T0. The comparison group showed the greatest potential as an antihyperuricemia agent compared to the EEDS dose group. The potential ability to reduce blood uric acid levels in the comparison group was not significantly different from the EEDS group in all test groups. This shows that the EEDS groups with doses of 100 mg/kg BW, 200 mg/kg BW and 400 mg/kg BW were able to show the same antihyperuricemia effect as the comparator (allopurinol) with the same onset of therapy. This is in accordance with previous studies which showed that bay leaf extract was effective in significantly reducing uric acid levels in test animal models (Hidayah et al., 2018; Norihsan & Megantara, 2018; Sahensolar et al., 2023) .

DISCUSSION

Based on Figure 1 above, hyperuricemia measurements at T1 and T2 showed that all EEDS dose groups and the comparison group had shown a significant decrease in blood uric acid levels compared to the induction group ($p < 0.05$) starting from T0. The comparison group showed the greatest potential as an antihyperuricemia agent compared to the EEDS dose group. The potential ability to reduce blood uric acid levels in the comparison group was not significantly different from the EEDS group in all test groups. This shows that the EEDS groups with doses of 100 mg/kg BW, 200 mg/kg BW and 400 mg/kg BW were able to show the same antihyperuricemia effect as the comparator (allopurinol) with the same onset of therapy. This is in accordance with previous studies which showed that bay leaf extract was effective in significantly reducing uric acid levels in test animal models (Hidayah et al., 2018; Norihsan & Megantara, 2018; Sahensolar et al., 2023). Hyperuricemia is an independent risk factor for diseases such as gout, chronic kidney disease, hypertension, cardiovascular and cerebrovascular diseases, and diabetes; and is also an independent predictor of premature death. Hyperuricemia is caused by impaired purine metabolism, which is characterized by increased serum uric acid levels. Although commonly used urate-lowering drugs such as allopurinol, febuxostat, and benzbromarone have some effectiveness, long-term use of these drugs causes significant side effects (Liu et al., 2023; Porth, 2015).

Allopurinol is a specific inhibitor and substrate for the xanthine oxidase enzyme. This drug functions as a substrate analog that will occupy the active site of the xanthine oxidase enzyme. Allopurinol is a purine analog. In the liver, allopurinol will be metabolized by xanthine oxidase, resulting in its active metabolite, oxypurinol (alloxanthine) which also has the ability to inhibit xanthine oxidase (Suhendi et al., 2011) . This indicates that uric acid biosynthesis is inhibited, so that uric acid levels in plasma will decrease. Pharmacokinetics of allopurinol almost 80% absorbed after oral administration, like uric acid, allopurinol is metabolized by xanthine oxidase itself, the resulting compound is allopurinol which can maintain the ability to inhibit xanthine oxidase and has a fairly long working period so that allopurinol is sufficient to be given only once a day (Brunton et al., 2008; Department of Pharmacology and Therapeutics, 2016; Pacher et al., 2006) . The EEDS group with doses of 100mg/kg BW, 200mg/kg BW, and 400mg/kg BW showed no significant difference in antihyperuricemic potential. Increasing the dose of the drug should increase the response that is proportional to the increased dose, but with increasing dose the increase in response will eventually decrease, because the dose has been reached that can no longer increase the response. The active compound contained in EEDS that is thought to play a role in lowering blood uric acid levels is flavonoids. Flavonoids

4 are reported to inhibit the action of the xanthine oxidase enzyme, thereby reducing excess uric acid levels. Xanthine oxidase is an enzyme that converts hypoxanthine to xanthine and xanthine to uric acid (Hidayah et al., 2018; Umamaheswari et al., 2013).

CONCLUSIONS

Ethanol extract of bay leaves has the potential as an antihyperuricemia agent comparable to the comparator used (allopurinol). The group of ethanol extract of bay leaves with a dose of 100 mg/kgBW showed the best effectiveness in reducing blood uric acid levels in test animals.

REFERENCE

Ariyanti, R., Wahyuningtyas, N., Arifah, D., & Wahyuni, S. (2007). The Effect of Giving Bay Leaf Infusion (Eugenia polyantha Wight) on Reducing Blood Uric Acid Levels in Male White Mice Induced with Potassium Octonate. *56 Pharmacon* , *8* (2), 56–63.

Brunton, L., Parker, K., Blumenthal, D., & Buxton, I. (2008). *Goodman & Gilman's: Manual of Pharmacology and Therapeutics* . Mc Graw Hill Medical. https://doi.org/10.1036/0071443436

Darussalam, M., & Rukmi, Dwi Kartika. (2019). *The Role Of Boiled Water Of Syzygium Polyanthum Leaves In Decreasing Hyperuricemia Levels* . *September* .

Department of Pharmacology and Therapeutics, FKU (2016). *Pharmacology and Therapy* (RNI Gunawan, Sulistia G; Setiabudy (ed.); 6th ed.). FK UI Publishing Agency.

Dira, D., Fitrianda, E., & Sari, N. (2015). Antihyperuricemia Activity Test of Ethanol Extract of Mangosteen Peel (Garcinia mangostana L.) and Asam Gelugur fruit (Garcinia atroviridis Griff. ex. T. Anders.) In Vitro. *Scientia: Journal of Pharmacy and Health* , *4* (2), 66. https://doi.org/10.36434/scientia.v4i2.5

Hidayah, N., Hasanah, F., Gunawan, M., & Lestari, A. (2018). Antihyperuricemia Effectiveness Test of Bay Leaf Extract (Syzygium polyanthum Wight.) On Male Mice Induced by Chicken Liver Juice and Potassium Oxonate. *Jurnal Saintika* , *18* (1), 24–31.

Hidayat, R., & Wulandari, P. (2021). The Effect of Syzygium polyanthum Extract in Lipid Profile of Hypercholesterolemic Animal Model. *Journal of Hunan University （Natural Sciences）* , *48* (5).

Liu, H.B., Yang, M., Li, W., Luo, T., Wu, Y., Liu, T., Luo, Y., Huang, XY, & Zhang, Y.L. (2023). Dispelling Dampness, Relieving Turbidity and Dredging Collaterals Decoction, Attenuates Potassium Oxonate-Induced Hyperuricemia in Rat Models. *Drug Design, Development and Therapy* , *17* (August), 2287–2301. https://doi.org/10.2147/DDDT.S419130

Muammar, Y. (2014). Potential of Indonesian Biodiversity as Xanthine Oxidase Inhibitor and Antigout. *Lanthanida Journal* , *1* (1).

Nadhifah, G., & Hidayati, N; Suhendy, H. (2021). Antihyperuricemic activity of several mango leaf extracts (Mangifera indica L.) var Cengkir on male white Wistar rats induced by potassium oxonate. *Pharmacoscript* , *4* (2), 163–172.

Ningtiyas, IF, & Ramadhian, MR (2016). Effectiveness of Bay Leaf Extract to Reduce Uric Acid Levels in Gout Arthritis Patients. *Medical Journal of Lampung University* , *5* (3), 105–110.

Norihsan, M., & Megantara, S. (2018). Review: Activity Test and Pharmacological Effects of

Bay Leaves (Eugenia Polyantha). *Farmaka* , *16* (3), 44–54.

Nur, K., & Sumiwi, SA (2020). Activity of Various Plants as Antihyperuricemia. *Farmaka* , *17* , 33–49.

Pacher, P., Nivorozhkin, A., & Szabó, C. (2006). Therapeutic effects of xanthine oxidase inhibitors: Renaissance half a century after the discovery of allopurinol. *Pharmacological Reviews* , *58* (1), 87–114. https://doi.org/10.1124/pr.58.1.6

Papadakis, M. A., & Mcphee, S. J. (2019). Current Medical Diagnosis & Treatment—2019. In *Mc Graw Hill Education Lange* (Fifty Eight, Vol. 3, Issue 1). Mc Graw Hill Education Lange. https://doi.org/10.1097/00004836-198103000-00028

Porth, C. M. (2015). Essentials of Phatophysiology Concepts of Alteres Health States. In *Woltres Kluwer: Vol. Edition 4* (4th ed.). Wolters Kluwer.

RI, K. (2019). Basic Health Research 2018. In *Health Research and Development Agency* . https://doi.org/10.12688/f1000research.46544.1

Saharuddin, M; Titawanno, J. (2019). Antihyperuricemia Effectiveness Test of Bay Leaf Extract (Syzygium polyanthum Wight.) On Male Mice (Mus musculus) Induced by Chicken Liver Juice and Potassium Oxonate. *Journal of Pharmacy and Sciences* , *11* (2), 60–69.

Sahensolar, M., Queljoe, E. De, & Sumantri, S. (2023). Antihyperuricemic activity test of bay leaf (Syzgium polyanthum) ethanol extract on white rats (Rattus norvegicus) Antihyperuricemic activity test of bay leaf (Syzgium polyanthum) ethanol extract on white rats (Rattus norvegicus). *Pharmacon* , *12* (1), 108–113.

Singh, J. A., & Gaffo, A. (2020). Gout epidemiology and comorbidities. *Seminars in Arthritis and Rheumatism* , *50* (3), S11–S16. https://doi.org/10.1016/j.semarthrit.2020.04.008

Somalinggi, YL, Maloa, BR, Suarti, ON, Bani, D., Nofinita, M., Lau, N., Josafat, T., Putra, D., & Virginia, DM (2023). Effectiveness of Bay Leaf Extract (Syzygium polyanthum) in Overcoming Gout in Indonesia. | *Pharmaceutical Journal* , *19* (2), 221–229. https://doi.org/10.22146/farmaseutik.v19i2.74044

Suhendi, A., Nurcahyanti, Muhtadi, & Sutrisna, EM (2011). Antihyperuricemia activity of black cumin water extract (Coleus ambonicus Lour) in male mice of the balb-c strain and its standardization. *Indonesian Pharmaceutical Journal* , *22* (2), 77–84.

Umamaheswari, M., Madeswaran, A., & Asokkumar, K. (2013). Virtual screening analysis and in-vitro xanthine oxidase inhibitory activity of some commercially available flavonoids. *Iranian Journal of Pharmaceutical Research* , *12* (3), 317–323.

Wariki Maria C; Ealeleng, BJ; Pandelaki, K. (2022). Association between serum uric acid level and peripheral arterial disease. *E-Clinic* , *10* (2), 298–305. https://doi.org/10.1016/j.atherosclerosis.2006.12.029

Yanti, P., Subarnas, A., & Renggana, H. (2021). Review: Antihyperuricemia Activity of Several Plants from Garut Arboretum. *Jurnal Pharmascience* , *8* (2), 17. https://doi.org/10.20527/jps .v8i2.9101