Effectiveness of Bay Leaf Extract (*Syzygium polyanthum*) on Uric Acid and Cholesterol Levels in Caffeine-Induced Male Mice (*Mus musculus*)

Fahrul Andika Pratama[1], Salma Aisyafalah[1], Rochmah Kurnijasanti[2]*
[1]Laborant of Veterinary Medicine, Universitas Airlangga, [2]Division of Basic Veterinary Medicine, Faculty of Veterinary Medicine, Universitas Airlangga, Surabaya, East Java, Indonesia.
Corresponding author: rochmah-k@fkh.unair.ac.id

ABSTRACT

Bay leaf (*Syzygium polyanthum*) is one of the plants from Indonesia that has the potential to be used as a raw material for herbal medicine. Pharmacologically, bay leaves containing flavonoids have been shown to have antioxidant activity, which can reduce hyperuricemia and blood cholesterol levels. This study aims to determine the effectiveness of bay leaf extract in reducing uric acid and cholesterol levels in the blood of mice induced by caffeine. The mice tested animals were divided into six groups, namely a positive control group of uric acid, a positive control of cholesterol, where a positive control of uric acid was given allopurinol and a positive control of cholesterol was given simvastatin, a negative control was given Na-CMC 1%, and a group that was given bay leaf extract in different dose levels, namely P1 was given 20 mg/kg BB, P2 was given 40 mg/kg BB, and P3 was given 80 mg/kg BB. The parameters used were the decrease in blood uric acid and cholesterol levels caused after the treatment was measured using a POCT strip test for uric acid and cholesterol. The data obtained were statistically processed using the One-Way Anova test. The results of the Anova test showed a significant difference ($p<0.05$) in the data on uric acid and cholesterol levels. Then continued with the results of Duncan's test to see the most effective dose level for bay leaf extract in reducing uric acid and cholesterol levels. In Duncan's test results, it was found that the P3 group of mice with a dose of 80 mg/kg BB was the most effective dose level in reducing uric acid and cholesterol levels in the blood of mice induced by caffeine.

Keywords: bay leaf, uric acid, cholesterol, caffeine, flavonoids

Received: 20-08-2024 **Revised:** 30-09-2024 **Accepted:** 30-11-2024

INTRODUCTION

Bay leaf (*Syzygium polyanthum*) of the myrtaceaea family is one of the plants from Indonesia that has the potential to be used as a raw material for herbal medicines. People have used bay leaves as a remedy for hyperglycemia (diabetes mellitus), hypertension, gout, antidiarrhea, lowering cholesterol levels, and gastritis. Pharmacologically, bay leaf has been proven to be antioxidant, antidiarrheal, antibacterial, lowers blood cholesterol levels, antiglycemia, and antihypertensive activity (Malik and Ahmad, 2013). By the POM Agency, bay leaf is designated as one of nine superior medicinal plants that have been researched or clinically tested to overcome certain health problems (Ana Fitri, 2007).

Indonesian people use bay leaves to flavor dishes. This is because of the fragrant and fresh aroma of bay leaves. This plant usually grows wild in forests, both in lowlands and mountainous areas. Bay leaves are very useful for treating gout. The parts of the tree that can be used as medicine are leaves, bark, roots, and fruits. The effect of bay leaves is as a urinary decay and pain reliever. The chemical content contained

in this bay plant includes saponins, triterpenoids, flavonoids, polyphenols, alkaloids, tannins, and essential oils consisting of sesquiterpenes, lactones, and phenols (Sutanto T, 2003).

There are many medicinal plants used for anti-hyperuricemia. One of the plants used as a traditional medicine to lower uric acid levels is the bay plant (*Syzygium polyanthum*). The parts of the plant used are fresh or dried leaves. Bay leaves have various medicinal properties that can be used in daily life. In addition to overcoming gout, bay leaves can also be used as a remedy for high cholesterol (Backer CA, 1963).

Uric acid is a substance resulting from the breakdown of purine or a waste product in the body, which is the result of catabolismmepurine assisted by the enzymes guanase and xanthine oxidase. This uric acid is carried to the kidneys through the bloodstream to be excreted with urine, if there is a disorder of uric acid elimination through the kidneys caused by a decrease in uric acid secretion into the renal tubules, there will be an increase in uric acid levels in the blood, this is a condition called hyperuricemia (Saputra R, 2008).

Hyperuricemia is a condition in which blood uric acid levels increase above normal by more than 7 mg/dl. Hyperuricemia can be caused by increased uric acid metabolism (overproduction), decreased uric acid excretion (underexcretion), or a combination of both (Putra TR, 2006). The prevalence of hyperuricemia in the community is estimated to be between 2.3% to 17.6% where it is found in 24.5% of men and 23.9% of women (Wortman RL, 2005). Hyperuricemia is a risk factor for the onset of gout arthritis, gout nephropathy, or kidney stones and a risk factor for ischemic heart disease (Kelley WN and Wortman RL, 1997).

Based on previous research, decocta (juice in water made from natural ingredients boiled at a temperature of 90 0C to 98 0C with a duration of 30 minutes) bay leaf at a dose of 1.25 g/kg BB, bay leaf infusion at a dose of 5.0 g/kg BB, and bay leaf ethanol extract at a dose of 420 mg/kg BB were able to reduce uric acid levels in serum blood whose results are equivalent to allopurinol at a dose of 10 mg/kg BB (Soedarsono, 2004). The flavonoid content in bay leaves also has activity as an antioxidant that can inhibit the action of the xanthine oxidase enzyme so that the formation of uric acid is inhibited (Utami IW, 2008).

One of the main causes of the increased incidence of coronary heart disease is cholesterol. Cholesterol comes from high-fat foods. In general, the diet in Indonesia is more dominant in carbohydrates than fat. However, the daily fat intake in Indonesian people comes more from cooking oil. Consumption of cooking oil that can cause coronary heart disease from year to year (Rustika, 2002).

The flavonoids in bay leaf extract contain a lot of antioxidants that can lower cholesterol levels and triglyceride levels in the blood, protect arteries from damage, reduce the amount of cholesterol deposits on the endothelial surface of arterial blood vessels. Animal studies have shown that flavonoids can lower lipid peroxidation in mice. According to previous research, flavonoids work as a cholesterol lowering by inhibiting cholesterol synthesis as an inhibitor of cholesterol formation enzymes (English, 2004).

From several previous research results, bay leaf extract can reduce uric acid levels and cholesterol levels because of the flavonoid content in bay leaf extract, which can inhibit the action of xiantin oxidase in uric acid and also inhibit cholesterol synthesis in cholesterol. So, it is necessary to research whether it is true that bay leaf

extract can reduce uric acid levels and cholesterol levels in the blood of caffeine-induced mice.

METHODS

Sampling of bay leaves

Population: Bay plants are found in almost all regions of Indonesia. A sample of bay leaf powder (*Syzygium polyanthum*) was obtained at the Indoplant Jogjakarta Store.

Sample processing

The samples of bay leaf powder (*Syzygium polyanthum*) that have been taken are washed using running water then drained and dried in a dryer. After drying, it is stored in a closed container, then ground in a machine until it is fine into powder.

Sample extraction

The extraction method used in this study is maceration. Sample of bay leaf powder (*Syzygium polyanthum*) weighed as much as 1 kilogram then put into a maceration container, then added ethanol filter, closed and left for 3x24 hours protected from light, while stirring occasionally. Then it is filtered and then separated between the pulp and filtrate. The ethanol extract solution in the rotary evaporator is then dried until a viscous extract is obtained.Detailed and clear explanation of research design, number of samples, treatment methods, materials used and work methods performed, including statistical methods and an explanation of animal ethical behavior certificates if necessary. The working method presented contains sufficient information to enable the study to be repeated successfully.

Animals

The experimental animals used in this study are male mice with a body weight of 20-30 grams. Before being used as experimental animals, all mice were kept for approximately one week to adjust the environment, control their health and weight, and standardize their diet. The food used is standard feed.

Dosage determination

The allopurinol dose used was 100 mg/kg BB for humans, and simvastatin was 10 mg/kg BB. The doses of bay leaf extract given to the animals in the study were concentrations of 20 mg/Kg BB, 40 mg/Kg BB and 80 mg/Kg BB.

Caffeine administration

In this test, efforts were made to increase uric acid levels and blood cholesterol levels by inducing mice with caffeine at a dose of 37.8 mg/kg BB orally.

Experimental animals

Before the trial animals are given treatment, they are first weighed for adjustment of the dose given. Each time they will be given treatment, the animal is fasted first for 12 hours to empty the stomach, so that the preparation is also better, because there is no interaction between food and medicine. Before being treated, mice were first measured for uric acid and cholesterol levels because they were used as a comparison between before treatment and after treatment. After that, the mice were made hyperuricemia and high cholesterol mice by induction using caffeine at a dose of 37.8 mg/kg BB for 6 consecutive days in all treatment groups, then their uric acid and cholesterol levels were measured. Furthermore, each group was given bay leaf extract to the P1, P2 and P3 mouse groups for 9 days, then the next day their uric acid and cholesterol levels were checked with a uric acid and cholesterol strip POCT tool.

Each mouse was given the following treatment: (Group I) Negative control, given Na CMC 1% orally, (Group II) Positive control, who were given

allopurinol at a dose of 0.39 mg/30 g BB orally, (Group III) Positive control, who were given simvastatin at a dose of 0.039 mg/30 g BB orally, (Group IV) Given bay leaf extract (*Syzygium polyanthum*) 20 mg/kg BB orally, (Group V) Given bay leaf extract (*Syzygium polyanthum*) 40 mg/kg BB orally, (Group VI) Given bay leaf powder extract (*Syzygium polyanthum*) 80 mg/kg BB orally.

Data analysis

The target sample processing technique is seen from the changes that occur in mice after measuring uric acid and cholesterol levels. Data Analysis Data analysis is determined by statistical methods.

RESULT AND DISCUSSION

This study used 30 male mice, with a body weight of 20-30 grams induced by caffeine and experiencing hyperglycemia and hypercholesterol. The mice were divided into 6 groups, namely the gout-positive control group, the cholesterol-positive control group, where the gout-positive control was given allopurinol and the cholesterol-positive dick was given simvastatin, the negative control was given Na-CMC 1%, and the group that was given bay leaf extract in 3 different dosage levels, namely P1 was given 20 mg/kg BB, P2 was given 40 mg/kg BB, and P3 was given 80 mg/kg BB. After that, all mice were weighed to determine the dose given to each of the mice. After that, before the treatment, all mice were checked for uric acid and cholesterol levels using POCT, then the mice were fasted for 12 hours the next day, then the treatment was carried out by being given caffeine induction for 6 days, in a row and then the uric acid and cholesterol levels were measured again to see the effect of caffeine administration on mice. After that, the mice were fasted again for 12 hours before being given bay leaf extract, after 12 hours the mice were ready to be given bay leaf extract for 9 consecutive days, then after that the mice were measured again for uric acid and cholesterol levels to see the effect on the administration of bay leaf extract.

The data from the study was in the form of analysis of uric acid and blood cholesterol levels in mice using the One-Way Anova test. This chapter will also present a discussion of the results of research data analysis. Furthermore, the researcher conducted a normality test first to determine the distribution of data distribution as a condition for the parametric test (one way anova).

Table 1. Results of normality test in gout using Test of Homogeneity of Variances

	Levene Statistic	**df1**	**DF2**	**Sig.**
Before Treatment	0.813	4	20	0.532
After Being Given Caffeine	1.615	4	30	0.209
After Being Given An External Greeting	2.026	4	20	0.129

December 2024, Vol.13 No.2, 68-80
Online pada https://e-journal.unair.ac.id/JBMV

Table 2. Test results One Way Anova at the level of uric acid in mice

		Sum of Squares	Df	Mean Square	F	Sig.
Before treatment	Between Groups	0.038	4	0.010	0.906	0.479
	Within Groups	0.212	20	0.011		
	Total	0.250	24			
After being given caffeine	Between Groups	2.658	4	0.665	73.844	0.000
	Within Groups	0.180	20	0.009		
	Total	2.838	24			
After being given an external greeting	Between Groups	0.568	4	0.142	7.634	0.001
	Within Groups	0.372	20	0.019		
	Total	0.940	24			

Table 3. Duncan Post hoc test results on uric acid levels in mice, before treatment

Group	N	$Subset\ for\ alpha = 0.05$
		1
P2	5	0.6800
K-	5	0.7200
K+	5	0.7200
P3	5	0.7200
P1	5	0.8000
Sig.		0.1120

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

Table 4. Duncan Post hoc test results on uric acid levels in mice, after being given caffeine

Group	N	Subest for alpha = 0.05		
		1	2	3
K+	5	0.7800		
K-	5		1.4400	
P2	5		1.5000	
P3	5			1.6400
P1	5			1.6800
Sig.		1.000	0.329	0.513

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

Table 5. Duncan Post hoc test results on uric acid levels in mice, after being given bay leaf extract

Group	N	Subest for alpha = 0.05	
		1	2
P2	5	0.5800	
K+	5	0.6400	
P3	5	0.6400	
K-	5		0.8800
P1	5		0.9600
Sig.		0.519	0.365

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

Table 6. Results of normality test on cholesterol using Test of Homogeneity of Variances

	Levene Statistic	df1	DF2	Sig.
Before Treatment	2.449	4	20	0.080
After Being Given Caffeine	0.088	4	20	0.985
After Being Given An External Greeting	1.640	4	20	0.203

Table 7. Test results One Way Anova on mice vein cholesterol

		Sum of Square	Df	Mean Square	F	Sig.
Before treatment	Between Groups	93.360	4	23.340	2.099	0.119
	Within Groups	222.400	20	11.120		
	Total	315.760	24			
After being given caffeine	Between Groups	2814.160	4	703.540	73.285	0.000
	Within Groups	192.000	20	9.600		
	Total	3006.160	24			
After being given an external greeting	Between Groups	936.240	4	234.060	18.576	0.000
	Within Groups	252.000	20	12.600		
	Total	1188.240	24			

Table 8. Results of Duncan's Post hoc test on cholesterol levels in mice, before treatment

Group	N	Subest for alpha = 0.05	
		1	2
K-	5	56.6000	
K+	5	58.8000	58.8000
P1	5	59.4000	59.4000
P3	5		61.4000
P2	5		62.0000
Sig.		0.223	0.179

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

Table 9. Results of Duncan's Post hoc test on cholesterol levels in mice, after being given caffeine

Group	N	Subest for alpha = 0.05	
		1	2
K+	5	59.4000	
P1	5		83.2000
P3	5		86.0000
P2	5		86.2000
K-	5		87.4000
Sig.		1.000	0.062

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

Table 10. Results of Duncan's Post hoc test on cholesterol levels in mice, after being given an external greeting

Group	N	Subest for alpha = 0.05		
		1	2	3
K+	5	61.2000		
P3	5	63.0000		
P2	5		68.6000	
P1	5		71.6000	
K-	5			78.2000
Sig.		0.432	0.196	1.000

Means for groups in homogeneous subsets are displayed.
a. Uses Harmonic Mean Sample Size = 5.000.

The table above shows the normality test value of the research data, which can be seen in the Sig. > (alpha, 0.05) column, then the data is normally distributed, then a different test is carried out One Way Anova.

The table above shows that in the group before the treatment, the value of sig. 0.479 means that there is no real difference because the value on sig. p > 0.05. For the group after being given caffeine and after being given bay leaf extract, there was a significant difference, because the values of both were sig. p < 0.05.

Furthermore, to find out the group that has the most significant influence, a further Duncan Post hoc test was carried out.

In Table 2, the results of the one-way anova test on uric acid levels in mice before treatment showed no significant difference, so in the follow-up test, the Duncan test in the group before treatment did not have a significant impact, and in the P1 group was the group with the highest uric acid levels in the group before treatment.

In the group after being given caffeine, there was a real difference in each group. In the Duncan test table, the K- and P2 groups have similarities, in P3 and P1 there are also similarities, namely having high uric acid levels compared to others, and the P1 group has the highest uric acid level values compared to other groups after being given caffeine.

In the group after being given bay leaf extract, there was also a real difference in each group. In the Duncan test table of the P2, K+ and P3 groups, there are similarities with low uric acid values, while in K- and P1 there are also similarities with high uric acid values and the P1 group has the highest uric acid level value compared to others after being given bay leaf extract while P2 has the lowest uric acid level value.

The Table 6 shows the normality test value of the research data, which can be seen in the Sig. > (alpha, 0.05) column, then the data is normally distributed, then a one-way anova differential test is carried out.

The table above shows that in the group before the treatment, the value of sig. 0.119 means that there is no real difference because the value on sig. $p > 0.05$. For the group after being given caffeine and after being given bay leaf extract, there was a significant difference, because the values of both were sig. $p < 0.05$. Furthermore, to find out the group that has the most significant influence, a further Duncan Post hoc test was carried out.

In Table 8, the results of the one-way anova test on cholesterol levels of mice before treatment showed that there was no real difference, so in the follow-up test, the Duncan test in the group before treatment did not have a significant impact on the results of the study.

In the group after being given caffeine, there was a noticeable difference. In the Duncan test table, the K+ group has the lowest cholesterol level value, at P1, P2, P3, K- is the group with high cholesterol level values, and the K- group has a higher cholesterol level value than others after being given caffeine.

In the group after being given bay leaf extract, there was also a real difference in each group. In the Duncan test table of the K+ group, P3 has similarities with low cholesterol values, while in P2 and P1 there are also similarities with higher cholesterol values than the previous group, and the K- group has the highest cholesterol level values compared to others after being given bay leaf extract.

This study uses the caffeine induction method which is a preclinical test that is closer to the actual state of gout and cholesterol sufferers. Caffeine can increase uric acid levels in the presence of a methyl group that will be oxidized by the enzyme xanthin oxidase to form uric acid in the body (Artini, et al 2012). Likewise in cholesterol, caffeine can also increase blood cholesterol levels and increase a person's risk of heart disease, a study in Australia has proven that coffee containing caffeine can affect high cholesterol levels (Waspadji et al, 2003).

Bay leaf extract is made using the extraction method because this method is a way to withdraw the soluble chemical content so that it is separated from the insoluble material with liquid solvents. This study only examined the

results of bay leaf extraction which affected reducing uric acid and cholesterol levels in the blood of caffeine induced mice of 37.8 mg/kg BB. Based on previous research, it has been shown that bay leaf ethanol extract can reduce uric acid and cholesterol levels in the blood which is supported by the presence of flavonoid compounds contained in it which are anti-inflammatory and antioxidant (Sinaga AF et al, 2014).

According to Falconer (1981), mice as experimental animals are very practical for quantitative research, because of their easy reproduction, besides that mice can also be used as model animals to study selection for quantitative traits. To minimize biological variation, researchers control several control variables. The control is carried out by using test animals that are more or less the same biological variation, including with a body weight of about 20-30 grams, male sex and also placed in the same cage and then fed the same feed. This is done so that the condition of the test animals is the same and to reduce the influence of the food consumed on the test preparation given in the study. To reduce stress levels, test animals were adapted to laboratory conditions for 7 days.

This study was conducted to see the effect of reducing bay leaf extract on uric acid and cholesterol levels in mice. The doses used in this study were 20 mg/kg BB, 40 mg/kg BB, 80 mg/kg BB. In addition, 3 groups of experimental animals were also used for control, namely positive control of uric acid, positive control of cholesterol and negative control. According to Budiharto (2008), the control group is used to ensure that the test results are not affected by other factors that can affect the test results. Positive control of uric acid is allopurinol 0.39 mg/30g BB, while for positive cholesterol control is simvastatin 0.039 mg/30g BB, and negative control is Na CMC 1%.

In this study, there was an activity of decreasing uric acid and cholesterol levels in the blood of mice from bay leaf extract which previously had an increase in uric acid and cholesterol levels in the blood of mice after being induced by caffeine. This can be seen from the results of the research above, and because of the content of bay leaf extract, namely flavonoids. It is suspected that the flavonoids contained in this plant have the effect of reducing uric acid and cholesterol levels in the mice's blood. The flavonoid content in bay leaves also has activity as an antioxidant that can inhibit the action of the xanthine oxidase enzyme so that the formation of uric acid is inhibited (Utami IW, 2008). Likewise, cholesterol levels also decreased because according to previous research, flavonoids work as a cholesterol lowering by inhibiting cholesterol synthesis as an inhibitor of cholesterol formation enzymes (English, 2004).

Research conducted on the measurement of uric acid levels in each group varies in uric acid levels, this can be seen from Appendix 3. Results of uric acid level measurement. After that, the data was processed using SPSS 24.0 using the one-way anova test, so the results were obtained on the blood uric acid levels of mice, namely in the group before the treatment was obtained in the group before the treatment value of sig. 0.479, meaning that there was no real difference because the value of sig. $p > 0.05$ so it did not have a significant effect on the research, because in this case the researcher only looked at the initial uric acid level before the treatment and the uric acid level of the mice Before treatment, the level of uric acid value is very diverse. In the group after being given caffeine, there was an increase in uric acid levels compared to before the

treatment. Caffeine is used as an inducer of gout because caffeine contains methylxanthin which is eliminated through the liver and excreted through urine in the form of uric acid. Caffeine can increase uric acid levels in the presence of a methyl group that will be oxidized by the enzyme xanthin oxidase to form uric acid in the body (Artini, et al 2012). This can be seen in Table 3 Duncan test results in the group after being given caffeine. In the K- and P2 groups, there is a similarity in having low uric acid levels, while in P3 and P1 there is also a similarity, namely having a high uric acid level value compared to others, but the P1 group has the highest uric acid level value compared to other groups after being given caffeine. While in the group after being given the P2, K+ and P3 group extracts, there were similarities with low uric acid values, while in K- and P1 there were also similarities with high uric acid values, but the P1 group had the highest uric acid level values compared to others after being given bay leaf extract, while P2 had the lowest uric acid level values.

In the results of the research carried out on the measurement of cholesterol level examination, each group of cholesterol levels also varies, this can be seen from Appendix 3. Results of cholesterol level measurement. After that, the data was processed using SPSS 24.0 using One Way Anova Test Blood cholesterol levels of mice were in the group before treatment obtained in the group before treatment with Sig values. 0.119 means that there is also no real difference because the value on sig. P > 0.05 so it did not have a significant effect on the study, and also the researcher only looked at the initial cholesterol level before the treatment and the cholesterol level of the mice before the treatment were very diverse. Seen in Table 8 The results of the Duncan test in the group after being given caffeine experienced an increase in cholesterol levels, and in the K+ group had the lowest cholesterol level value, in P1, P2, P3, K- was the group with high cholesterol level values, and the K- group had a higher cholesterol level value than others after being given caffeine. In the group after being given bay leaf extract in the Duncan test table of the K+ group, P3 had similarities with low cholesterol values, while in P2 and P1 there were also similarities with higher cholesterol values than the previous group, and the K- group had the highest cholesterol level values compared to others after being given bay leaf extract.

From the results that have been presented above, it can be seen that all doses of bay leaf extract turn out to have the effect of reducing uric acid and cholesterol levels in the blood of mice whose uric acid and cholesterol levels previously increased due to caffeine induction. This can be seen in the test table One Way Anova which experienced a noticeable difference in uric acid and cholesterol levels. That bay leaf ethanol extract can reduce uric acid levels in the blood and cholesterol supported by the presence of flavonoid compounds contained in it which are anti-inflammatory (Sinaga AF, et al 2014). The flavonoid content in bay leaves also has activity as an antioxidant that can inhibit the action of the xanthine oxidase enzyme so that the formation of uric acid is inhibited (Utami IW, 2008). Likewise, cholesterol levels also decreased because according to previous research, flavonoids work as a cholesterol lowering by inhibiting cholesterol synthesis as an inhibitor of cholesterol formation enzymes (English, 2004).

In gout, the P3 group with a bay leaf extract dose of 80 mg/kg BB was the most effective dose, because judging

from the activity after being given caffeine, the P3 group experienced an increase in high uric acid levels, then given bay leaf extract, the P3 group experienced a significant decrease compared to other groups. Likewise, the cholesterol level of the P3 group with a dose of 80 mg/kg BB is also the group with the most effective dose, because after being given caffeine, the P3 group experienced an increase in high cholesterol levels, then after being given bay leaf extract, the P3 group decreased. So in the P3 group which was given a dose of 80 mg/kg BB on both uric acid and cholesterol became the most effective dose in reducing uric acid levels and blood cholesterol levels of mice.

CONCLUSION

Bay leaf extract (*Syzygium polyanthum*) has the effect of significantly lowering uric acid and cholesterol levels in caffeine-inuced mice. Bayside leaf extract treatment group (*Syzygium polyanthum*) namely the P3 group with a dose of 80 mg/kg BB is the most effective dose in lowering caffeine-induced uric acid and cholesterol levels.

REFERENCES

Ana Fitri, 2007. "Pengaruh Penambahan Daun Salam (Eugenia Polyantha Wight) Terhadap Kualitas Mikrobiologis, Kualitas Organoleptis dan Daya Simpan Telur Asin pada Suhu Kamar", Skripsi (Surakarta : Program studi strata satu Universitas Sebelas Maret, 2007), hlm. 13.

Andri, W.Y. 2007. Produksi Mencit Putih (*Mus Musculus*) dengan Substitusi Bawang Putih (*Allium Sativum*) dalam Ransum, Skripsi. Fakultas Peternakan Institut Pertanian Bogor. P. 3-5.

Ariyanti, R., Wahyuningtyas, N., dan Wahyuni, A.S., 2007, Pengaruh Pemberian Infusa Daun Salam (Eugenia Polyantha Wight) terhadap Penurunan Kadar Asam Urat Dalam Darah Mencit Putih Jantan yang Diinduksi Potasium Oksonat, Pharmacon, 8 (2),56-63.

Artini NPR, Wahyuni. 2012. Ekstrak Daun Sirsak (Annona Muricata L. terhadap penurunan Kadar Asam Urat Darah Tikus Wistar. Jurnal Kimia Fakultas MIPA Universitas Udayana. Vol 6: 121-137.

Azizahwati, Wiryowidagdo, S., dan Prihandini, K., 2005. Efek penurunan kadar asam urat dalam darah pada tikus jantan dari rebusan akar tanaman akar kucing (Acalypha indica Linn), Jurnal Bahan Alam Indonesia, 4(1):213-218.

Backer CA. Flora of java (spermatophytes only). Noordhoff-Groningen: Bakhuizen van den Brink RC Jr; 1963.

Badan POM RI., 2004, Monografi Ekstrak Tumbuhan Obat Indonesia.

Budiharto, 2008. Metodologi Penelitian Kesehatan dengan Contoh Bidang Ilmu Kesehatan Gigi. Jakarta: Penerbit IKAPL. hlm. 51.

Depkes, RI., 2000. Parameter Standar Umum Ekstrak Tumbuhan Obat. Direktorat Jendral Pengawasan Obat dan Makanan, Direktorat Pengawasan Obat Tradisional. Jakarta.

Departemen Kesehatan Republik Indonesia. 2008. Farmakope Herbal Indonesia. Jakarta.

English J, 2004.New dietary supplement shows dramatic effects in lowering cholesterol, ldl, trigliserydes. 4 Januari 2011.

Falconer, D.S. 1981. Introduction to Quantitative Genetics. Longman, London and New York.

Kelley WN, Wortmann RL. Gout and hyperuricemia. Dalam: Kelley WN,

editor.Textbook of rheumatology. Edisi 5. Philadelphia: WBSaunders Company; 1997. hlm.1314-50.

Malik, A., dan Ahmad, A.R. 2013. Antidiarrheal Activity of Etanolic Extract of Bay Leaves (*Syzygium Polyanthum* Wight). Int. Res. J. Pharm. 4(4) : 106-108.

Nety Wulandari,"Pengaruh Pemberian Ekstrak *Syzygium polyanthum* Terhadap Produksi ROI Makrofog Pada Mencit BALB/c yang Diinokulai Salmonella typhimurium", Skripsi (Semarang : Universitas Diponegoro, 2006), hlm.19.

Nijveldt, R. J., Nood, E. V., Hoorn, D. E. V., Boelens, P. G., Norren, K. V., dan Leeuwen, P. A. V. 2001. Flavonoids: A Review of Probable Mechanisms of Action and Potential Applications. American Journal of Clinical Nutrition 74(4): 418-425.

Price & Wilson. 2005. Patofisiologi : Gangguan Sistem Kardiovaskular. Jakarta : EGC pp. 582-283.

Putra TR. Hiperurisemia. Dalam: Sudoyo AW, editor. Buku ajar penyakit dalam.Edisi 4. Jakarta:Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Indonesia; 2006. hlm. 1213-7.

Rizqiana Dewi, Aktivitas Antioksidan dan Sitotoksisitas Metabolit Sekunder Daun Salam (*Syzygium polyanthum* Wight) Dan Daun Jati Belanda (Guazuma ulmifolia Lamk.), Skripsi, (Bogor : Program studi strata satu Institut Pertanian Bogor, 2012), hlm. 3.

Rustika. 2002. Pola konsumsi minyak goreng keluarga dan peningkatan risiko kolesterol. http://digilib.litbang.depkes.go.id. 16 Desember 2010.

Saputra R. Efek fraksi etil asetat ekstrak etanol daun salam (*Syzygium polyanthum* Wight.) terhadap penurunan kadar asam urat darah mencit putih jantan galur balbc yang diinduksi kalium oksonat [skripsi]. Surakarta: Universitas Muhammadiyah Surakarta; 2008.

Silbernagl, S. 2006. In: Silbernagl, S., Lang, F. editor. Teks dan Atlas Berwarna Patofisiologi. Jakarta : EGC.

Sinaga AF, Widdhi B, Widya AL. Uji efek etanol daun salam terhadap penurunan kadar asam urat tikus putih jantan galur wistar yang diinduksi potassium oksalat. Manado: Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Sam Ratulangi; 2014.

Smith John B dan Mangkoewidjojo Soesanto. 1988. Pemeliharaan, Pembiakan, dan Penggunaan Hewan Percobaan di Daerah Tropis Jakarta. Universitas Indonesia Salemba 4. Hlm. 37 -48.

Soedarsono, et al. Tumbuhan obat pusat. Jillid 2. Yogyakarta: Studi Obat Tradisional; 2002. hlm. 174.

Sudarmi. 1997. Kafein dalam Pandangan Farmasi. Medan: Fakultas Matematika dan Ilmu Pengetahuan Alam (FMIPA) Universitas Sumatera Utara (USU).

Sutanto T. Asam Urat deteksi, pencegahan, pengobatan. Yogyakarta: Penerbit BukuPintar; 2003.

Utami IW. Efek fraksi air ekstrak etanol daun salam (*Syzygium polyanthum* Wight.) terhadap penurunan kadar asam urat pada mencit putih (*Mus musculus*) jantan galur balb-c yang diinduksi dengan kaliumoksinat [skripsi].Surakarta: Universitas Muhammadiyah Surakarta; 2008.

Wachjudi G, et al. Diagnosis dan terapi penyakit reumatik. Jakarta:Sagung Seto; 2006.

Wade A, Waller PJ. Handbook of pharmaceutical excipient second

sedition. London The Pharmaceutical Press. 1994.

Waspadji S, dkk 2003. Indeks Glikemik Berbagai Makanan Indonesia. Jakarta : Fakultas Kedokteran Universitas Indonesia.

Wartini, N.M. 2009. Senyawa Penyusun Ekstrak Flavor Daun Salam (Eugenia polyantha Wight) Hasil Distilasi Uap Menggunakan Pelarut n-Heksana dan Tanpa n-Heksana. Agrotekno 15(2): 72- 77.

Wortman RL. Disorders of purine and pyrimidine metabolism. Dalam: Kasper DL, editor.Harrison's principles ofinternal medicine. Edisi 16. Volume 2. New York McGraw-Hill; 2005. hlm. 2308-13.

***