Anti-hyperuricemia Effect of Water Fraction Cinnamon (*Cinnamomum burmannii* (Ness & T. Ness) Blume) on White Male Rats

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Abstract: Hyperuricemia is a condition of increased concentration of uric acid in the blood. Cinnamon bark (*Cinnamomum burmannii* (Ness & T. Ness) Blume) has been used empirically to decrease uric acid levels. This research is to determine the effect of water fraction from cinnamon bark as anti-hyperuricemia. For being in hyperuricemia condition, the rats were provided with high-purine food and potassium oxonate 50mg/200gBW as an uricase inhibitor. As many as 4,108 mg dose/200gBW of Allopurinol was used as a comparison for positive control. The dose of cinnamon bark used was 104 mg/200g BW for the first group, 208 mg/200g BB for the second group and 416 mg/200gBW for the third group. The result shows that the second group can lower uric acid level (58,87%) and has a similar result with the positive group (P>0.05). It concludes that the water fraction of cinnamon bark has antihyperuricemia effect.

1 INTRODUCTION

Uric acid is the final product formed from purine compounds (adenine and guanine), produced in tissues containing xanthine oxidase enzymes especially in the liver and small intestine. Under normal circumstances, uric acid may be excreted through the kidneys. But if the synthesis of uric acid is too much or its excretion through the kidneys is too small, then the levels in the blood will increase. The crystalline crystals that are difficult to dissolve in all body fluids settle in the joints and tissues and cause inflammation. Deposition of urate crystals may also occur in the kidney and will eventually damage the organ (Murray, *et al*. 2005).

Uric acid disease is commonly experienced by people today, and mostly suffered by the productive age group, of 30-50 years old, which can decrease work productivity. Pathophysiological condition occurs increased when levels of uric acid in blood has increased beyond the normal limit, which is called hyperuricemia. In hyperuricemia there will be an accumulation of uric acid crystals in the joints causing inflammation and pain or pain known as gout (Priyanto 2008).

The main factor that affect hyperuricemia incidence is unhealthy diet of high protein, especially of animal protein that contains a lot of high purine, which results in hyperuricemia. Gout disease is a state of human metabolic disorder suffered by more than 2 billion in the world and can attack men, women, old or young, even young children (Kramer 2002 in Astuti 2011). Pirai or gout is characterized by recurrent episodes of acute arthritis due to precipitation of monosodium urate crystals in joints and surrounding tissues (Katzung *et al*. 2012). This disease usually occurs due to an increase in uric acid levels in the blood up to normal > 7 mg/dl in men and > 6 mg/dl in women (Dipiro *et al*. 2005). Hyperuricemia may occur due to excessive production of uric acid, reduced uric acid expenditure, or a combination of both (Christian 2013).

Today's society believes that treatment by using natural ingredients is a natural way in the treatment of gout (Kamalia 2010). In general, to overcome hyperuricemia disease, synthetic drugs such as allopurinol have been used, but allopurinol can cause side effects such as skin, stomach, intestine and blood disorders. To overcome this, alternative

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medicine using medicinal plants are developed such as cinnamon bark (Private and Ernawati 2010).

Cinnamon is one of the many spices found in Indonesia and has been used since the past as cooking herbs and traditional herbs (Gunawan 2011). The chemical content of cinnamon bark includes essential oils, tannins, saponins and polyphenols (Depkes 2008). According to Astawan (2011) in Tuiyo *et al*. (2013), compounds with high polyphenol content have high antioxidant activity as well, to inhibit xanthine oxidase enzyme. Xanthine oxidase enzyme serves to catalyze the changes of purine into uric acid. By inhibiting the xanthine oxidase enzyme, the formation of uric acid will be hampered as well.

2 MATERIALS AND METHODS

The plant material used is cinnamon bark (*Cinnamomum burmannii* (Ness & T. Ness) Blume) obtained from BALITRO Bogor, West Java. The chemicals used are 96% Ethanol, water, potassium oxonate, chicken liver juice, allopurinol, and TBHBA uric acid kit reagent. The test animals in this study were Sprague Dawley male, white rats weighing between 200-300 grams and about three months old. The tool used is Spuit 1 cc, oral sonde for rats, mouse scales, clinical spectrophotometers, and glass tools commonly used in chemical laboratories.

2.1 Determination of Plants

Cinnamon bark is detected in Herbarium Bogoriense, Balitbang Botany-Puslitbang Biologi LIPI-Cibinong.

2.2 Extraction

Rough powder of cinnamon bark extracted with 96% ethanol (3 x 24 hours) is macerated at room temperature. The solvent is then evaporated with a rotary evaporator at a temperature of 50 ° C to obtain a viscous extract.

2.3 Fractination

The extract was fractionated with aquadest and n-hexane (1: 1). The fraction of the obtained aquadest is then fractionated with ethyl acetate (1: 1).

2.4 Phytochemical Screening

Phytochemical screening was performed on thick and viscous extracts to determine the presence of secondary metabolite compounds such as alkaloid compounds, polyphenols, flavonoids, saponins, tannins, quinones, and terpenoids.

2.5 Determination of Drying

Determination of weight loss on drying was carried out on extracts and cinnamon bark fractions dried at 105^0C for 30 minutes in the oven. Drying is done until the weight is fixed. The bottle is left closed and cools in the desiccator to room temperature.

Table 1: Treatment group of anti-hyperuricemia fraction of cinnamon water

Groups Day	I	II	III	IV	V	VI
Treatment	Normal Control	Positive Control	Negative Control	Dose I	Dose II	Dose III
Day 0	Rat Fasting, then the blood was taken to know the beginning of uric acid levels					
Day 1-14		The rats were orally fed with high purine				
Day 9		Intraperitoneal Induction of potassium oxonate				
Day 9	The blood was taken two hours after administering potassium oxonate (to check the increase of uric acid levels in blood)					
Day 10	-	Administered Allopurinol	Administered Na CMC 0,5%	The fraction of cinnamon bark dose I	The fraction of cinnamon bark dose II	The fraction of cinnamon bark dose III
Day 14	Induction of potassium oxonate after administering of the fraction, blood sample was taken 2 hours after the last fraction was administered (to check the lowering of uric acid levels or effect of the fraction of cinnamon bark)					

2.6 Anti-Hyperuricemia Activity Testing

Rats were divided into control groups and test groups, each group consisting of 4 rats (Table 1).

3 RESULTS AND DISCUSSION

3.1 Determination of Simplicia

The bark of cinnamon is determined in Herbarium Bogoriense, Balitbang Botany-Puslitbang Biologi LIPI-Cibinong. The results of determination show that the plants used are Cinnamon (*Cinnamomum burmannii* (Ness & T. Ness) Blume).

3.2 Ethanol Extract of Cinnamon Bark

Cinnamon bark (2 kg) extracted with 96% ethanol (3 x 24 hours) yielded a thickened extract of 521.6 g (yield of 26.08%). The viscous extract obtained is dark brown, smells distinctive and tastes bitter.

3.3 Weight Loss on Drying

Weight loss on drying are carried out to determine residual substances that evaporate at 105ºC. Based on the test it is known that drying drift contained in ethanol extract 96% cinnamon bark is 5.28%, and in cinnamon, bark fraction is 4.48%.

3.4 Water Fraction of Cinnamon Bark

The cinnamon bark extract 451 g was fractionated with aquadest, n-hexane and ethyl acetate yielding 81.52 g of water fraction (yield of 18.07%).

3.5 Secondary Metabolites in The Extract

The phytochemical screening showed that in the cinnamon extract and fraction there were various secondary metabolites, shown in Table 2.

3.6 Anti-Hyperuricemia Activity

Increased uric acid level was performed by giving 15 g/15ml dose of chicken liver juice 2 times a day, but the provision of chicken liver juice did not provide significant results, due to mammals with lower levels, there are uricase enzymes that play a role in the process of uric acid conversion to become allantoin. Allantoin is more soluble in water and more easily excreted by the body of the mammal (Katzung *et al*. 2012). Therefore, it takes the induction of potassium oxonate to help increase uric acid levels in mice to be more significant. Potassium oxonate is used as a competitive inhibitor of uricase enzyme work so that uric acid in rat blood can accumulate cause hyperuricemia condition, the dose used is 50mg/200gBW through intraperitonial.

To find out the anti-hyperuricemia activity, cinnamon bark water was extracted to decrease uric acid level in mouse blood, a variation of the dose given was 104 mg/200g BW, 208 mg/200g BW, and 416 mg/200g BW 2 times a day.

The results of uric acid levels (table 3) obtained showed that on Day 9 there was a significant increase with chicken liver juice and oxonate potassium induction, and decreased on Day 14 after administration of ethyl acetate fraction of cinnamon bark.

The normal group is a reference for the occurrence of uric acid level on the Day 9, which is decreased on the Day 14 without any treatment. In the positive control, there was an increase of uric acid on the Day 9 after the induction of potassium oxonate which was decreased on the Day 14 after the administration of allopurinol with the dose of 4,108 mg/200 gBW for 5 days. In the negative

Table 2: Phytochemical screening of cinnamon extract and fraction

No	Phytochemical screening	Observation (colours)	Extract of ethanol 96%	Fraction of Ethyl Acetate
1	Alkaloid	Old brown	+	+
2	Flavonoid	Red	+	+
3	Saponin	Foam	+	+
4	Tanin	Black	+	+
5	Steroid dan terpenoid	-	-	-

Information :
(+) = Exist, (-) = no

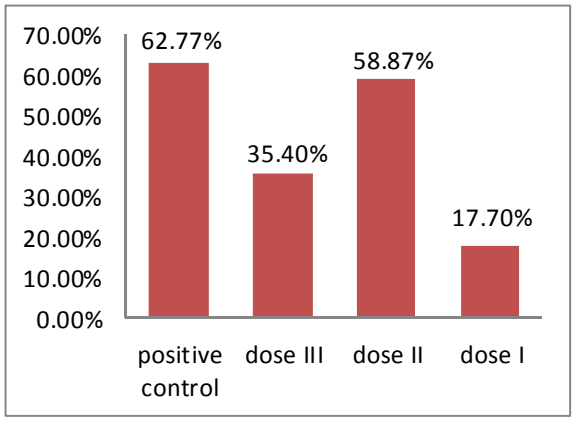

Figure 1: Percentage of uric acid levels. Positive control (allopurinol 4,108 mg/200 gBW). Dose I (Fraction of cinnamon bark water 108 mg/200 gBW). Dose II (Fraction of cinnamon bark water 204 mg/200 gBW). Dose III (Fraction of cinnamon bark water 416 mg/200 gBW)

group, there was also an increase of uric acid on the Day 9 after the induction of potassium oxonate which then decreased on the Day 14 after the administration of Na CMC 0.5% for 5 days. In the

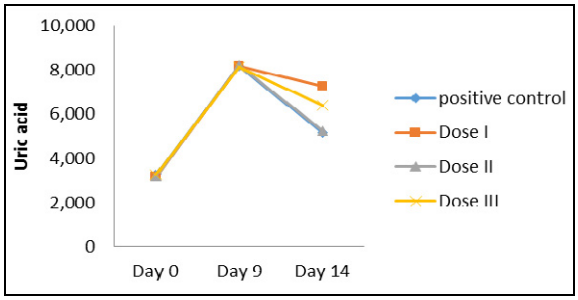

Figure 2: The lowering of uric acid levels

dose groups, there were increases of uric acid level on the Day 9 after the induction of potassium oxonate and then decreased on the day 14 after the administration of all the dose fractions (I, II, III) for 5 days.

The highest percentage belonged to the positive control that is Allopurinol with percentage of 62,77%. Second activity belonged to the group of dose II with percentage equal to 58,87%. Third activity belonged to dose I with the percentage equal to 35,40%, followed by group Dose III with the percentage of 17.70% (figure 1).

Table 3: Uric acid levels in rats

Time	Groups					
(Day)	Normal	Negative	Positive	Dose I	Dose II	Dose III
0	3.30	3.46	3.36	3.25	3.29	3.17
	3.03	3.21	3.23	3.12	3.16	3.21
	3.12	3.50	3.49	3.07	3.12	3.47
	3.21	3.11	3.09	3.32	3.21	3.24
Average	3.16	3.32	3.29	3.19	3.19	3.27
Deviation (SD)	0.10	0.16	0.15	0.10	0.06	0.12
9	3.28	8.16	8.24	8.42	8.26	8.21
	3.19	8.27	8.31	8.17	8.16	8.06
	3.42	8.38	8.42	8.09	8.31	8.31
	3.36	8.24	8.26	7.96	8.14	7.94
Average	3.31	8.26	8.16	8.16	8.22	8.13
Deviation (SD)	0.09	0.08	0.07	0.17	0.07	0.14
14	3.46	8.15	5.12	7.41	5.21	6.58
	3.17	8.20	5.08	7.26	5.17	6.75
	3.24	8.08	5.16	7.32	5.43	6.09
	3.28	8.01	5.29	7.13	5.24	6.23
Average	3.60	8.13	5.16	7.28	5.26	6.41
Deviation (SD)	0.11	0.07	0.08	0.10	0.10	0.26

Information :
Group I : normal control (no treatment)
Group II : positive control (allopurinol 4,108 mg/200 g BW)
Group III : negative control (Na CMC 0,5%)
Group IV : dose I (104 mg/200 gBW)
Group V : dose II (208 mg/200 gBW)
Group VI : dose III (416 mg/200 gBW)

Data on the average decrease in uric acid levels obtained from each group (Table 3) showed that allopurinol could decrease uric acid levels by 62.77% (Figure 2). The activity approaching allopurinol is owned by the dose group II which has a percentage of 58.87%. In this case, it can be seen that doses I, II and III have the ability to decrease uric acid levels in the blood of white male rats, but dose II can lower uric acid levels to near normal, although not equivalent to allopurinol and normal controls. This is probably due to the concentration of nutritious compounds contained in the bark of cinnamon varies, and the timing of the fraction is too short.

The data of uric acid levels (table 3) obtained then tested with normality and homogeneity test. Normality test using Kolmogorov Smirnov Test showed that normal distributed data with significance value 0,419 ($p \geq 0,05$) data is said to be normally distributed because having significance value more than 0,05. While the homogeneity test results showed a significance value of 0.114 ($p \geq 0.05$) so that the data can be said to be homogeneous. Further data were analyzed using one-way variance analysis to know that the data obtained had significant differences between groups with days of each treatment.

The uric acid level data was continued with the Tukey test to determine the significant differences in each group. From the Tukey test it was found that there was a significant difference between the dose I test group and all groups, as well as on the dose III test. However, in the dose II test group (204 mg/200 gBW) there was no significant difference with the positive group (allopurinol 4.108 mg/200 gBW) which means that the dose II had an anti-hyperuricemia activity not much different from the positive control group Phytochemical screening tests show that cinnamon bark contains alkaloids, flavonoids, saponins and tannins.

4 CONCLUSIONS

Based on the results of the study it can be concluded that cinnamon bark fraction has activity with dose II (204 mg/200gBW) as the most effective, successfully decreasing uric acid level in rat blood by a percentage equal to 58,87%. Normality test using Kolmogorov Smirnov Test showed that the data was normally distributed with significance value of 0.419 ($p \geq 0,05$), and the homogeneity test showed significance value of 0,114 ($p \geq 0,05$) which indicates that the data can be classifield as homogeneous.

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REFERENCES

Astuti, D. 2011. Efek Anti-hyperuricemia Kombinasi Ekstrak Air Kelopak Rosella (*Hibiscus sabdariffa* L) dan Akar Tanaman Akar Kucing (*Acalypha indica* L) Pada Tikus Putih Jantan yang Diinduksi Kalium Oksonat. *Skripsi*. Universitas Indonesia.

Departemen Kesehatan Republik Indonesia. 2008. Farmakope Herbal Indonesia, Edisi 1. Jakarta. Hlm. 41

Gunawan, ES. 2011. Pengaruh Pemberian Ekstrak Kayu Manis (*Cinnamomum burmannii*) Terhadap Gambaran Mikroskopis Hepar, Kadar SGOT dan SGPT Darah Mencit BALB/C yang Diinduksi Paracetamol. Universitas Dipenogoro. Semarang.

Kamalia, L. 2010. Efektivitas fraksi etanol daun kembang sungsang *(Gloriosa superba* L.*)*. *Skripsi*. Universitas Muhammadiyah Prof. Dr. Hamka. Jakarta.

Katzung, B.G., Masters, S.B. & Trevor, A.J. 2012. Basic & Clinical Pharmacology, 12 Ed., New York: McGraw-Hill.

Kristiani, Risa D. 2013. Pengujian Aktivitas Anti-hyperuricemia Ekstrak Etanol Akar Pakis Tangkur (*Polypodium feei*) Pada Mencit Jantan. *Skripsi*. Fakultas Farmasi Universitas Padjajaran, Jatinangor.

Murray, RK, Granner DK, Mayes PA, Rodwell VW. 2005. *Biokimia Harper, Edisi 25.* Terjemahan dari harper biochemistry oleh andy hartanto. Buku Kedokteran EGC, Jakarta.

Pribadi, FW dan Ernawati, DA. 2010. Efek Catechin Terhadap Kadar Asam Urat, *C–Reactive Protein* (CRP) dan Malondialdehid Darah Tikus Putih (*Rattus norvegicus*) Hiperurisemia. Jurnal *Mandala of Health*, Vol 4 No. 1. Universitas Jendral Soedirman. Purwokerto.

Priyanto. 2008. Farmakologi Dasar. Lilian Batubara (eds). Leskonfi. Jakarta.

Tuiyo KI, Hamsidar Hasan dan Moh Adam M. 2013. Uji Efek Ekstrak Etanol Kayu Manis (*Cinnamomum burmannii*) Terhadap Tikus Putih Jantan (*Rattus norvegicus*). *Jurnal Skripsi*. UNG. Gorontalo.