ISSN 0303 - 7932

FOLIA MEDICA INDONESIANA

Vol. 45 No. 4 October – December 2009

International Online Distribution by ProQuest™
www.proquest.com

Folia Medica Indonesiana	Vol.45	No. 4	Page 244-323	Surabaya Oct-Dec 2009	ISSN 0303 - 7932

FOLIA MEDICA INDONESIANA

ISSN 0303 - 7932

Vol. 45 No. 4 October – December 2009

Medical journal, published by Airlangga University School of Medicine, Surabaya, publishing original basic medical and clinical articles presented as research articles and review articles

Published by : **GRAMIK (Graha Masyarakat Ilmiah Kedokteran)**
(Center for the Medical Scientific Community)
Quarterly (January -March, April -June, July -September, October -December)

Address : **Airlangga University School of Medicine**
Jl. Prof dr Moestop o 47 Surabaya 60131
Phone: 62 -31-5013749, 5020251 -3 ext. 135
Fax : 62 -31-5013749, 62 -31-5022472
E-mail: folia@fk.unair.ac.id

Subscription: Rp. 120.000,00/annum (US $ 50 for other countries outside Indonesia)h

Accredited no. 167/DIKTI/Kep/2007

FOLIA MEDICA INDONESIANA

ISSN 0303 - 7932

Vol. 45 No. 4 October - December 2009

CONTENTS

Folia Medica Indonesiana Vol. 45 No. 4 October – December 2009 : 249-252

UTILIZATION OF EXTRACT PHALERIA (*PHALERIA MACROCARPA*) AS À PRECAUTION AGAINST CARBON TETRACHLORIDE INDUCED HEPATOTOXICITY IN MICE

Reny I'tishom, Rochmah Kurnijasanti
Department of Medical Biology
Faculty of Medicine, Airlangga University

ABSTRACT

The hepatoprotective activity of extract of mahkota dewa fruit's (Phaleria macrocarpa) was investigated against Carbon Tetracloride (CCl4) induced hepatic damage. Carbon Tetracloride at a dose of 0,3 ml/kg body weight produced liver damage in mice as manifested by the rise in serum level of Glutamate Pyruvate Transaminase (GPT) and Glutamate Oxaloacetat Transaminase (GOT) to 31.4286 ± 2.4398 and 87.1429 ± 2.4398 respectively, compared to respective control values of 23.0000 ± 1.7889 and 39.0000 ± 3.6968. Pretreatment of mice with mahkota dewa fruit's extract at concentration of 2.5 ; 5; 10 mg/kg body weigth significantly prevent ($p < 0.001$) Carbon Tetracloride induced rise in serum enzymes and the estimated values of GPT was 27.2857 ± 1.9760 ; 22.8750 ± 2.1002 and 22.1667 ± 1.3239 respectively, and GOT was 53.0000 ± 8.6410 ; 45.1429 ± 3.4365 and 40.6667 ± 7.1740 respectively. The result indicate that the mahkota dewa fruit's (Phaleria macrocarpa) extract possesses hepatoprotetective activity which probably related to its antioxidant activity.

Keywords: *Phaleria macrocarpa, hepatotoxic*

Correspondence: Reny I'tishom, Department of Medical Biology, Faculty of Medicine, Airlangga University, Jl Prof. Dr. Moestopo 47, Surabaya 60131.

INTRODUCTION

Interest in using traditional medicine, in recent years tended to increase. This is because of fears of side effects brought about by modern medicine and also with the reasons easily obtained and relatively cheap (Hargono 1993). Phaleria (Phaleria macrocarpa) is one of the many plants used by communities as a traditional medicine to overcome the various complaints such as for diabetes, liver, antimicrobial, hypertension and cancer (Perry 1980). However, until now the scientific evidence from activists such materials has not been widely publicized by the experts.

Empirically, the crown of the gods are widely used to cure various diseases such as liver, cancer, heart disease, diabetes, gout, rheumatism, kidney, hypertension and others. From the very limited scientific research note that the chemical content of the crown of the god has a rich, where the levels of the chemical still has not been revealed.In the skin of the fruit and leaves contain alkaloids, saponins and flavonoids. Also in the leaves also contained polyphenols. While Lisdawati (2002) proved that crops containing Phaleria terpenoids, alkaloids, saponins and polyphenols. Plants that contain flavonoids, saponins, alkaloids, terpenoids, polyphenols in general have as cytotoxic and antioxidant effects. Flavonoid compounds including phytonutrients, phytonutrients are the active components of plants that function as antioxidants (Scholbe 2002). Physiological function of antioxidants is to prevent further damage cellular components as a result of chemical reactions involving free radicals (Young 2001).

Free radical production occurs continuously in all cells as part of normal cellular function. If there is excessive production of free radicals that may cause oxidative stress (Young 2001). Oxidative stress plays an important role in the pathophysiology of various diseases, one of the main pathogens cause liver disorders (Laura et al. 2004)

Liver is an organ that plays an important role in the process of metabolism and detoxification. Exposure by various toxic substances will enhance liver damage. Potential liver damage as it is the first organ exposed to gastrointestinal toxic materials. The process of metabolism by the liver will detoxify these substances, but the process can produce metabolites which are more toxic than the parent material (David & Thomas 1990).

In this study, as a model of liver disease, used hepatotoksin potent induction of carbon tetrachloride (CCL 4) in experimental animals (Pandit et al. 2004). CCL 4 is the prototype hepatotoxic substances most frequently used in research related to hepatotoxicity, because with small doses have shown a clear effect of the damage, available in pure form, can give the same

effect on different species and when given orally can cause damage More severe liver than other organs (Gitlin 1990). CCL 4 is a model of liver damage caused by free radicals. CCL 4 in particular require metabolic activation by cytochrome P450 enzymes in the liver. Activation will change the CCL 4 becomes more reactive and become more toxic metabolites, causing liver damage in experimental animals or humans. This is possible because the liver has a great ability to regenerate. To look at liver function, it can be done liver function tests.

Liver function tests can be classified based on liver secretion and excretion, metabolic function, enzyme activity and macroscopic anatomic/biopsy of the liver. Liver biopsy test results are often not comparable with the biochemical tests, because a lot of heart function that does not reflect changes in the structure of liver function that can be observed histologically. For that in determining the diagnosis of liver function should be a series of liver function tests. Tests based on enzyme activity is most often performed because it is more practical, one of which is the enzyme that includes an enzyme alanine transaminase and AST.

Based on the above background, in this study wants to prove whether the extract Phaleria (Phaleria macrocarpa), which have antioxidant roperties have preventive effects against hepatotoxicity in mice induced by CCL 4, by looking at the decline in ALT and AST levels of lood serum of mice . From this research can be obtained information and scientific data about the potential of the extract as a hepatoprotective Phaleria.

MATERIALS AND METHODS

The research design used is the type of experimental research using randomized, posttest only design.The population of the sample was male mice aged between 2-3 months and weighed between 20-30 grams obtained from the Center of Surabaya Veterinaria Farma. This study used seven samples for each group so that the overall sample size was 35 mice.

The method used was simple random sampling. Phaleria (Phaleria macrocarpa) that has been dried, is made of powder.

Powders that have been dried fruit (500 g) was extracted separately with methanol by vacuum evaporation techniques to extract the viscous extract obtained. Making solutions CCL 4. CCL fourth dose given 0.3 ml/kg BW and was diluted in olive oil with a ratio of 1:1.

In this experiment, 35 mice were randomly divided into five groups, each group contained seven mice. Prior treatment of mice are adapted for one week. haleria extract was administered orally once daily sonde. On Day 9 all groups (except group I) were given CCL 4 which has been dissolved in olive oil with a dose of 0.3 ml per kg body weight by intra peritoneal to make hepatotoksistas. Details of the distribution of the following groups: Group I: seven mice given the extract solvent and solvent Phaleria CCL 4 (negative control), Group II: seven mice were given the solvent extract Phaleria and CCL 4 0.3 ml/kg bw (positive control), Group III: seven mice were given extract Phaleria dose 2.5 mg/kg BW and CCL 4 0.3 ml/kg BW, Group IV: seven mice were given extracts of Phaleria a dose of 5 mg/kg BW and CCL 4 0.3 ml/kg, Group V: mice were given seven Phaleria extract at a dose of 10 mg /kg BW and CCL 4 0.3 ml/kg.

On Day 10 (24 hours after administration of CCL 4) done taking blood from the heart in all groups, each with as much blood drawn approximately 1 ml. Before blood sampling, experimental animals were kept during the first 12 ja, but keep drinking water provided. Blood is collected in serological tubes without anticoagulant and closed with a rubber cover. Furthermore, in centrifuge with 2000 rpm speed for 5 minutes. Serum obtained from centrifuging used as samples for examination of ALT and AST. Survey data in the form of ALT and AST levels were analyzed by ANOVA. If there are significant differences followed by Duncan's multiple range test using SPSS 10 for windows 2000.

RESULTS

The results that have been conducted using 35 male mice divided into five treatment groups showed that the extract with a concentration Phaleria 10, 5, 2.5 mg/kg could inhibit the increase in ALT and AST levels induced by carbon tetrachloride (CCL 4) dose of 0.3 ml/kg BW.

Data from the research results obtained are tabulated ALT levels as listed in Table 1.

Table 1 Average and Standard Deviation of the Various Treatment ALT Levels in Mice

Group	ALT Level (X ± SD) (mg/dl)
I	$23.0000^{a} \pm 1.7889$
II	$31.4286^{c} \pm 2.4398$
III	$27.2857^{b} \pm 1.9760$
IV	$22.8750^{a} \pm 2.1002$
V	$22.1667^{a} \pm 1.3239$

a. b. c Different superscript in the same column indicate a highly significant difference ($p < 0.01$)

Based on data analysis using the ANOVA program of SPSS 10 for windows on serum ALT of the results showed a significant difference ($p < .01$) among treatments. To determine whether there are significant differences between treatments then followed by Duncan's multiple range test. From the calculation results obtained by Duncan's multiple range test was highly significant difference between treatment. In Table 1 show that the group V (treated with extracts of Phaleria 10 mg/kg BW) produced the lowest ALT levels (22.1667 ± 1.3292). whereas there were highest in group II (treated with solvent extracts and CCL Phaleria 4 0.3 ml/kg. positive control) with ALT levels of 31.4286 ± 2.4398. ALT levels between treatment groups I. IV and V there was no significant difference. but significantly different from groups II and III. Based on these analysis results can be shown with bar charts as shown in Figure 1. which indicated that group V had the lowest ALT levels.

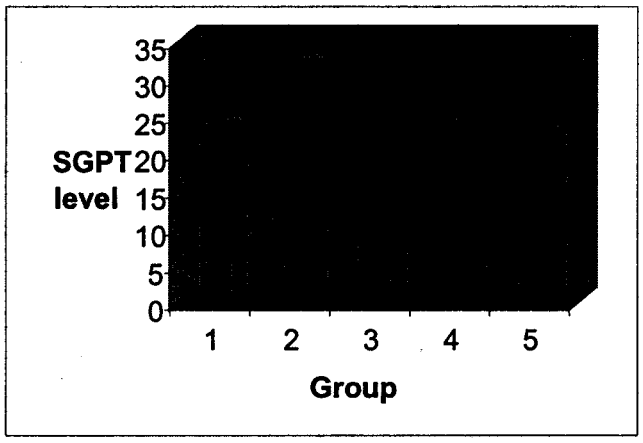

Figure 1. Influence Graph Phaleria extracts with various concentrations of the decrease in ALT levels induced by CCL 4 in mice.

The results Phaleria extract influence on serum AST CCL 4-induced mice. Can be seen in Table 2.

Table 2 Average levels of SGOT and standard deviation of various treatments on mice

Group	AST Level (X ± SD) (mg/dl)
I	$39.0000^{a} \pm 3.6968$
II	$87.1429^{c} \pm 2.4398$
III	$53.0000^{b} \pm 8.6410$
IV	$45.1429^{a} \pm 3.4365$
V	$40.6667^{a} \pm 7.1740$

a. b. c different superscript in the same column indicate a highly significant difference ($p < 0.01$)

Based on data analysis using the ANOVA program of SPSS 10 for windows on serum AST of the results showed a significant difference ($p < 0.01$) among treatments. To determine whether there is a significant difference between treatments then followed by Duncan's multiple range test. From the calculation results obtained by Duncan's multiple range test was highly significant difference between treatment. In Table 2 shows that the group I (only given the solvent extract and solvent Phaleria CCL 4/negative control) produced the lowest levels of SGOT (39.0000 ± 3.6968) which did not differ significantly with AST levels of group IV (Mahkota Dewa Fruit Extract 5 mg/kg BB) and group V (Mahkota Dewa Fruit Extract 10 mg/kg BW) whereas the highest AST levels found in group II (treated with solvent extracts of Phaleria and CCL 4 0.3 ml/kg/positive control) with AST levels 87.1429 ± 9.3350.

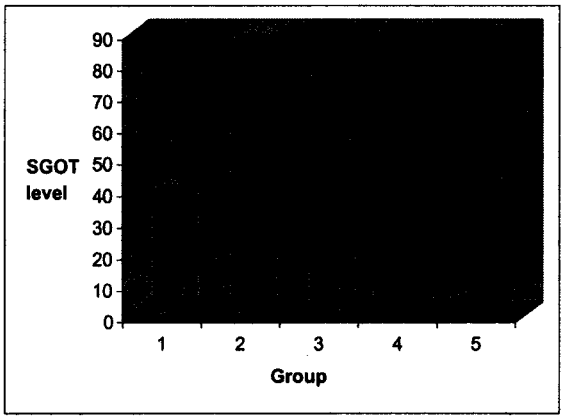

Figure 2. Influence Graph Phaleria extracts with various concentrations of the decrease in AST levels induced by CCL 4 in mice

Based on statistical analysis can be shown with bar charts as shown in Figure 2. which indicated that the group I have the lowest and highest levels of ALT is the group II.

DISCUSSION

Liver is one organ that plays a role in the protective function of the body against toxins and foreign objects into the body (detoxification). Liver plays a role in changing all foreign materials or toxins from outside the body. Foreign substances or toxins may take the form of food. medicines and other materials. can also be material from the body itself becomes inactive or less

toxic.

Detoxification ability is limited. so that not all incoming materials detoxified perfectly. but dumped in the blood and can cause damage to liver cells (David et al. 1990). In the detoxification function. compounds that have toxic properties of the body's cells by the liver changed into compounds that are no longer toxic and then the blood was brought into the kidney to excreted. and vice versa (Katzung 2001). Although the majority of pathological liver tissue disorder are severe. but clinical symptoms in patients can not always be observed. This is possible because the liver has a great ability to regenerate.

Liver has a large functional reserve. therefore new possibilities of liver function failure occurred after the majority (70%). liver parenchymal cells or hepatocytes were damaged. For that in determining the diagnosis of liver function should be a series of liver function tests. Tests based on enzyme activity is most often performed because it is more practical.

Based on the results of research on the use of extracts of Phaleria (Phaleria macrocarpa) as a precaution against hepatotoxicity of mice induced with carbon tetrachloride showed that the extract concentration Phaleria 2.5. 5 and 10 mg/kg can reduce levels of serum ALT and AST mouse blood. This is possible because the active material content of the extract Phaleria which have an antioxidant effect (Lisdawati 2002). Antioxidants are used as protection from CCL 4 liver cells which induces damage by breaking the chain reaction of lipid peroxidation. It has been stated that the peroxidation or covalent bond itself causes cell death. Antioxidants prevent the possibility of catastrophic necrosis of CCL 4. and through activities at the signal path tranduksi TNFα and perhaps also by preventing the occurrence of fibrosis and cirrhosis. This is in accordance with the work of vitamin E that is trusted as The most important lipophilic antioxidant in biological tissue. proved to be able to prevent acute damage induced by CCl4 by preventing lipid peroxidation by arresting CCl3OO • radicals and antioxidant activity of vitamin E can prevent binding transcription factor NF-kappa. activation of transcription factor AP-1 or expression of TNFα.

CONCLUSION

Based on the results of research on the use of extracts of Phaleria (Phaleria macrocarpa) as a precaution against induced hepatotoxicity Carbon tetrakloride (CCL 4) in mice. it is concluded that Phaleria extract (Phaleria macrocarpa) can reduce levels of serum ALT in mice induced by CCL 4. Phaleria extract (Phaleria macrocarpa) can lower blood serum levels of AST in mice induced by CCL 4. need to conduct further research the effect of extracts of Phaleria (Phaleria macrocarpa) is curative against carbon tetrachloride induced hepatotoxicity by looking at the decrease in ALT and AST levels of blood serum of mice.

REFERENCES

David. Z and T.D. Boyer. 1990. Hepatology A texbook of Liver Disease. Biopchemical Tests for Liver Disease. 2nd Ed. W.B. Saunders Company.

Gitlin. N. 1990. Clinical Aspects of Liver Diseases Caused by Industrial and Environmental Toxins. In (Zakim D. ed) Hepatology Textbook of Liver Disease. 2 nd ed. Philadelpia : WB Saunders Company.

Hargono. P. 1993. Perspektif pengembangan Obat Tradisional di Indonesia.

Katzung. B.G. 2001. Basic and Clinical Pharmacology. 8th ed. Lange Medical Book/Mc Graw-Hill. Medical Publishing Devision. USA.

Laura. C. Carlo Vascotto. Sebastian Calligaris. Gianluca Tell. 2004. The Importance of Redox State in Liver Damage. Annals of Hepatology.

Lisdawati. 2002. Buah Mahkota Dewa. Toksisitas. Efek antiokasidan bedasarkan uji penapisan Farmakologi. Universitas Gajah Mada.

Pandit. S. Sur . T.K. Jana. U. Debnath. P.K. sen. s and Bhattacharyya D. 2004. Prevention of Carbon Tetrachloride – Induced Hepatotoxicity in rat by Adhatoda Vasica Leaves. Indian Journal of Pharmakology. Vol 36.

Perry. L.M. 1980. Medicinal Plant of East and Southeast Asia Atributed Properties and Uses. MIT Press. London.

Scholbe. G. 2002. Diet: Past. Present and Beyond-Phytonutrient. 2 November 2003. http:// www.HolosticBird.com.

Young. I.S and J.V. Woodside. 2000. Antioxidant in Health and Disease. J. Clinical Pathology