BIOTOXIC OF GEMOR (*Nothaphoebe coriacea*) LEAVES FROM PEAT-SWAMP TUMBANG NUSA RESEARCH FOREST, CENTRAL KALIMANTAN, INDONESIA

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Abstract: The study aimed to evaluate the sub-acute toxicity effect of aqueous N. coriacea leaves extract to kidney and liver function. *The biotoxic study was conducted using male rats. In this study, the experimental animals received five different doses of aqueous N. coriacea leaves extract (0.1 mg, 1 mg, 10 mg, 100 mg, and 1000 mg per day) for 4 weeks via oral route. After treatment, the level of plasma ureum, creatinine, Aspartate Transaminase (AST) and Alanine Transaminase (ALT) level were measured. The results show that most of dose treatments of aqueous extract of N. coriacea leaves had not statistically effect on the level of the plasma ureum and creatinine except for dosage of 1000 mg. Similarly, the dose treatments of that extract did not statistically change the plasma AST and ALT, except on 100 and 1000 mg/kg of b.w extract dose. In conclusion, a short-term intake of N. coriacea leaves extract via oral route was not toxic to kidney and liver.*

Keywords: *N. coriacea, Kidney, Liver, Toxicity.*

INTRODUCTION

The Lauraceae family is one of the biggest group of the Laurales arrange including 50 genera and more than 2000 species. This plant family spread in tropical and subtropical from low- to high-lands area including Southeast Asia. This family can be perceived by its particular flower morphology.[1-2] The bark is smooth, rugged, and has numerous lenticels. The characteristics of this plant are yellow, orange, red, fragrant, or pink inner bark, simple leaves with several gland dots, and produced a distinctive aroma when the leaves are crushed.[2]

Kalimantan is one of the largest islands in Indonesia. In Kalimantan island, one of Lauraceae species was naturally found and has been exploited since 1970's for several industries, locally known as Gemor (*N. coriacea*).[3] It can be found in several district in Central Kalimantan, such as Palangkaraya, Pulang Pisau, and Gunung Mas.[4] There are two assortments of *N. coriacea*, i.e. trees having rather dull shading barks, which are anything but difficult to be peeled off, thick and create more bounteous of sticky-jam like sap, and trees having yellowish red barks, which are hard to be peeled off, slenderer and deliver less sticky-jam like sap. The population of trees having yellowish red bark is only 20% of the total number of *N. coriacea* trees observed in Central Kalimantan Province. However, local society prefer to gather the bark of *N. coriacea* rather than *N. umbelliflora*.[4] *N. coriacea* is additionally one of high temperate trees on the world trade and contended with another bark from another country like Taiwan, Singapore, and Japan.[5] The bark of *N. coriacea* is utilized as the fundamental crude material for mosquito repellent fabricate, incense for ceremonies and crude materials for stick.[4]

Besides the prospective raw material for industries, *N. coriacea* has several medical benefits. According to the previous study, the bark of *N. coriacea* has viral activity for influenza and herpes virus.[6] Arifin et al.[6] also reported that the different parts of *N. coriacea* (twig, bark, and leaves) have anti-inflammation activity. It is also reported that the bark, twig, and leaves of *N. coriacea* trees contain several phytochemical components. It contained alkaloid, steroid, flavonoid, saponin, triterpenoid, tannins, and phenolic compounds.[7] Suhartono et al.[8] has successfully reported that the aqueous extract of bark and leaves of *N. coriacea* has a significant inhibition effect to protect the glucose metabolism disturbance in liver of rats by Cd. Similarly, in another study, the administration of aqueous extract of *N. coriacea* leaves can improve the oxidative stress status in the brain of rats.[9]

Despite a lot of pharmacological studies of *N. coriacea*, there is no published study about the toxicity effect especially in liver and kidney, yet. Furthermore, a study about the toxicity effect and safety might be important to the development of *N. coriacea*. Because of that, this present study aims to investigate the subacute toxicity profile of aqueous extract of *N. coriacea* leaves in liver and kidney of rats.

RESEARCH METHODS

The *N. coriacea* leaves were collected on August 2015 in Forest for Specific Purposes (KHDTK), Central Kalimantan, Indonesia, located at latitude of is 3027'-30 59' S, 1130 2' 36"- 1140 44' 00" E, based on Global Positioning System (GPS) A bulk sample of *N. coriacea* leaves was obtained from sapling and poles. The collected leaves were then air-dried in darkness at room temperature. Afterward, the dried samples were made into a powder using a blender.

The extract was prepared using decoction-extraction. About 100 g of the shade-dried of seed and leaves were boiled for 30 min in 1000 ml of distilled water. The

mixtures were then allowed to be cool at room temperature, which were then filtered using Whatman no. 5 paper. The resulted solutions were then used in the experiment by following protocol section established by Suhartono et al.[9]

The rats were acclimatized in standard lab conditions for no less than 2 weeks before treatment. The rats were nourished with standard eat and were enabled free access to tap water. After that, an ethical approval was acquired from the Ethics Committee of Faculty of Medicine, Lambung Mangkurat University, Banjarmasin, South Kalimantan, Indonesia.

On the day ago of the 4th week, animals fasted overnight. Blood tests were after that gathered by cardiac puncture. The blood then centrifuged at 3000 rpm for 10 min. Serum was divide and assayed by using diagnostic kits for creatinine, blood urea, aspartate transaminase (AST), and alanine transaminase (ALT).[10] All the assays were led as stated by the manufacturers' direction book protocol.[11]

The Outcome results data were expressed as the mean±standard error of the mean (SEM). Statistical analysis was performed using SPSS statistical program version 16. One-way ANOVA test might have been utilized to parametric comparisons between the control and treatment groups and followed by post hoc Tukey HSD test. The differences were considered significant when the p-value was less than 0.05 ($p < 0.05$).

RESULTS AND DISCUSSION

The need of herbal drugs as an alternative for clinical therapy increases each year. The utilization of herbal drugs is based on long-term clinical experience. Although it has been used widely, the pharmacology and toxicity of these plants become subjects of interest from scientists. Many scientific efforts to investigate and validate the pharmacological properties and the toxicity of these medicinal plants have been conducted.[12] In the present study, we tested the potential toxicity of sub-acute exposure of N. coriacea leaves extract to kidney and liver function by measuring the level of the ureum, creatinine, aspartate transaminase (AST), and alanine transaminase (ALT).

Results of kidney function assesment by measuring the level of ureum and creatinine of animal samples were presented in figure 1 and 2, respectively. It showed that both serum levels of ureum, and creatinine were slightly increased in dosage of 100 and 1000 mg/kg b.w of extract, which was still categorized in normal range.[13-14]

Results of AST and ALT levels of the experimental animals examination are presented in in figure 3 and 4. It showed that extract treatments altered AST and ALT level in dose of 100 and 1000 mg/kg b.w for AST level, while the dose of 1, 100, and 1000 mg/kg b.w had the slight effect on the ALT level; although, these changes were still within the normal range. In addition, Nevin and Seckin measured serum ALT and AST levels in the Sprague Dawley rats. In their study levels of serum ALT and AST in healthy rats were 47.5±8.9 IU/l and 136.4±13.8 IU/l respectively. Young et al. evaluated the levels of markers of hepatotoxicity in Sprague Dawley rats and documented the levels of serum ALT (47±3.9) and serum AST (131±20.5) in healthy control group. The previous study measured the serum ALT and AST levels in healthy control as 29.5±7.5 IU/l and 137.3±11.8 IU/l respectively.[15]

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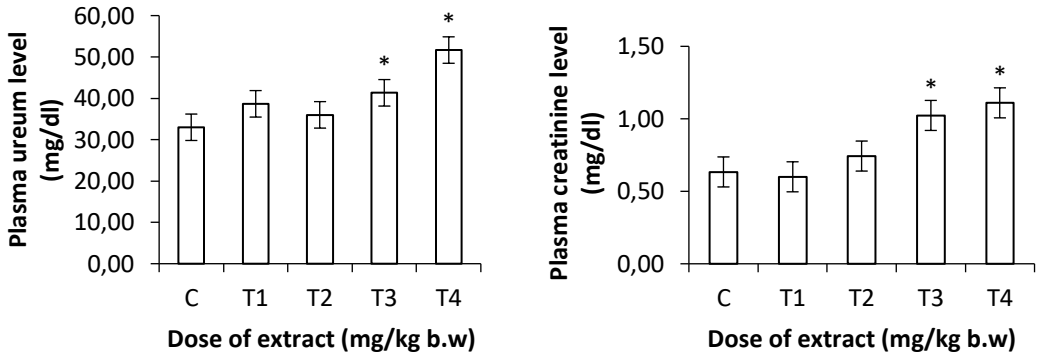

Figure 1. (a) Plasma ureum and (b) creatinine level in the animal samples after treated with various dose concentration (control: 0,1 mg/kg b.w; T1: 1mg/kg b.w; T2: 10 mg/kg b.w; T3 100 mg/kg b.w; and T4: 1000 mg/kgb.w) of Gemor extract. * P < 0.05 compared with respective with control group.

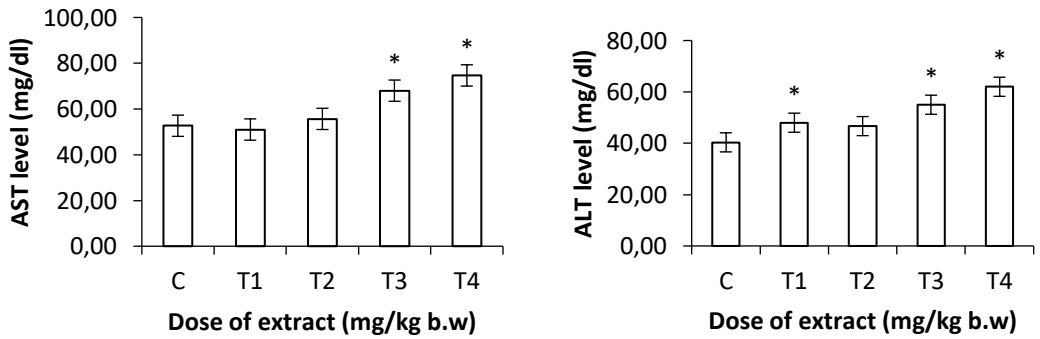

Figure 2. (a) Plasma AST and (b) ALT level in the animal samples after treated with various dose concentration (control: 0,1 mg/kg b.w; T1: 1mg/kg b.w; T2: 10 mg/kg b.w; T3 100 mg/kg b.w; and T4: 1000 mg/kgb.w) of Gemor extract. * P < 0.05 compared with respective with control group.

Damage and toxicity of a toxic substance can be seen from cell damage. The cell damage can be measured using several markers, and one of them is an enzyme. The level of an enzyme can increase since the existence of an enzyme leak due to cell damage. For the liver, the level of AST or serum glutamate oxaloacetate transaminase (SGOT), and ALT or serum glutamate pyruvate transaminase (SGPT) as an early marker of liver damage. The increasing of these two enzymes in the blood could be an indicator to liver damage.[16]

The measurement of ALT or both ALT and AST can be used in the diagnosis of cardiac or liver disease. ALT is the liver-specific enzyme; therefore it can also be detected when serum levels of both ALT and AST in liver cells become elevated due to the chronic disease processes. Increasing levels of ALT or AST or both of them may occur in common bile duct stone conditions, e.g. transient biliary obstruction; medications, e.g. acetaminophen; common

liver disease causes e.g. alcohol abuse, cirrhosis, hepatotoxins, viral hepatitis, steatohepatitis (fatty liver); uncommon liver diseases e.g. autoimmune hepatitis, hemochromatosis, alpha-1-antitrypsin deficiency and Wilson's disease.[17-18]

CONCLUSION

In conclusion, results of present study on the biotoxic analysis of aqueous extract of leaves of *N. coriacea* indicate that those extracts have a broad safety margin to liver and kidney with the range various concentration of dose treatments is between 0,1-1000 mg/kg b.w in experimental animals. This study may be useful used to complement other analysis in further preclinical pharmacological studies.

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