TOXICITY SUBCHRONIC ETHANOLIC EXTRACT OF MALAKA (Phyllanthus emblica) LEAVES ON LIVER FUNCTION OF MICE (Mus musculus): REVIEWED FROM SERUM BILIRUBIN LEVEL

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ABSTRACT

The aim of this research was to investigate the subchronic toxicity of ethanolic extract of malacca leaves (Phyllanthus emblica) on liver function by analyzing bilirubin level in mice blood (Mus musculus). Sixteen male mice weighing between 25-30 grams were used in this study. Ethanolic extract of malacca leaves was given orally once a day for 21 consecutive days. Mice were randomly divided into 4 groups of 4 mice each. Control group (P0) was given distilled water; group P1, P2, and P3 were administered with ethanolic extract of malacca leaves with the dose of 300 mg/kg bb, 600 mg/kg bb, and 1200 mg/kg bb, respectively. Blood samples were taken on day 21 after treatment to measure mice bilirubin level. The results showed that blood bilirubin level of mice in P0, P1, P2, and P3 were 1.1; 1.4; 1.4, and 1.4 mg/dl respectively. In conclusion, the administration of ethanolic extract of malacca leaves with repeated doses for 21 days does not have negative effect on mice liver.

Keywords: ethanolic extract, malacca leaves, liver function, bilirubin direct.

INTRODUCTION

Herbal medicines are often promoted as natural products which are safe to consume. However, some toxicity tests prove that some herbal products can cause a negative effect even toxic to the body. Toxicity test is an important method in determining the potency of a compound as a poison, to measure biological or environmental conditions, the appearance of toxic effects, and catalyze action (Wirasuta et al., 2007). Phyllanthus emblica is a material often used by the community as a traditional medicine. In India, this plant has been used to treat cancer, diabetes, liver, heart problems, and anemia (Khan, 2009). Biological activity is thought to be caused by the presence of bioactive compounds from secondary metabolites contained in them, especially compounds of the phenolic, flavonoid, and antioxidant groups are quite high (Liu et al., 2008). The previous research conducted by Jaijoy et al. (2010) revealed that malacca fruit water extract does not cause toxic effect on acute toxicity test. In chronic toxicity test of
Toxicity Subchronic Ethanolic Extract of Malaka (*Phyllanthus emblica*) Leaves

Malacca fruit water extract causing physiological changes of the experimental animal, decrease of organ size, and decrease of body weight, but still within normal limits. In another study conducted by Armansyah et al. (2016), also showed that acute toxicity test of malacca leaf ethanolic extract at dose of 16 g/Kg bw did not cause toxic effect in experimental animals. Thus, it is important to conduct the research on the effect of malacca leaves (*Phyllanthus emblica*) as herbal medicine when consumed continuously on blood chemistry components. Any ingredients that enter the body will undergo a pharmacokinetic process that is absorbed in the intestine, distributed throughout the body, then metabolized by the liver and excreted through bile or kidney (Suryati et al., 2016). Prolonged use of drugs can cause the gradual accumulation of metabolites in important organs, such as liver, gastrointestinal tract or kidneys. The organs will work hard to filter and remove compounds that are not needed by the body. This will cause a reaction of complications in these organs (Hidayatulloh and Susilaningsih, 2010).

**MATERIALS AND METHODS**

**Research Methods**

This study was a laboratory experimental research using one way pattern completely randomized design (CRD) consisting of 4 treatments groups with 4 replications each. A total of 16 mice weighing of 25-30 grams were divided randomly into 4 groups. Group I (P0) as a negative control was given distilled water; group II (P1), III (P2), and IV (P3) were given ethanolic extract of malacca leaves with dose of 300 mg/kg bb, 600 mg/kg bb, and 1200 mg/kg bb, respectively (Jaijoy et al., 2010).

**Research Procedure**

**Preparation of Malacca Leaf Extract**

Malacca leaves were obtained from the area of Sibreh, Aceh Besar, air dried at room temperature, then blended into powder using a blender. Malacca leaf powder was macerated in 96% ethanol solvent for a week, the solution was filtered using filter paper. The extract was evaporated using a rotary evaporator at a temperature ranging from 30-40°C until a viscous extract was obtained. The viscous extract is then suspended in 1% NaCMC.

**Measurement of Blood Bilirubin Direct Levels of Mice**

Mice were treated with ethanolic extract of Malacca leaves orally using gastric sonde once daily for 21 consecutive days. Blood was taken on day 21 after treatment for measurement of bilirubin direct levels (Suryati et al., 2016). Blood samples were collected from the orbital
Toxicity Subchronic Ethanolic Extract of Malaka (*Phyllanthus emblica*) Leaves

sinuses, subsequently put into the vacuum tube. Blood was centrifuged at a rate of 3000 rpm for 15 min. Then serum was used for the analysis of bilirubin direct levels. Measurement of bilirubin direct levels was carried out using a spectrophotometer at a wavelength of 505 nm.

**RESULTS AND DISCUSSION**

Liver is an important organ that functions to detoxify excess chemicals compound (Hernawati, 2012). Toxicant causes various types of toxic effect on several hepatic organelles, such as fatty liver, necrosis, cholestasis, and cirrhosis (Lu, 1995). Liver damage is characterized by hyperbilirubinemia, an increase in bilirubin level, which caused by the inhibition of bilirubin transport to the bile, thus it will accumulate in the blood. The increase of conjugated bilirubin level indicates a disturbance of the liver in the form of liver cell damage or bile ducts (Isna, 2015). Conjugated bilirubin in bile duct cannot be transported to the intestine, thus it will re-enter and absorb in the bloodstream. Damaged liver cells obstruct the biliary sinusoidal resulted in the increase of conjugated bilirubin level (Kee, 2007). The effect of malacca leaf ethanolic extract on direct bilirubin level in mice blood serum shows in Table 1.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>(mg/dl) ± SD</th>
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<tbody>
<tr>
<td>P0 (distilled water)</td>
<td>1.4 ± 0.45</td>
</tr>
<tr>
<td>P1 (Malacca leaf ethanolic extract dose of 300 mg/kg bw)</td>
<td>1.4 ± 0.51</td>
</tr>
<tr>
<td>P2 (Malacca leaf ethanolic extract dose of 600 mg/kg bw)</td>
<td>1.4 ± 0.54</td>
</tr>
<tr>
<td>P3 (Malacca leaf ethanolic extract dose of 1200 mg/kg bw)</td>
<td>1.4 ± 0.47</td>
</tr>
</tbody>
</table>

The results showed that bilirubin level of mice blood in P0, P1, P2, and P3 were 1.4; 1.4; 1.4, and 1.4mg/dl respectively. The bilirubin level from all treatment groups did not significantly different among treatment. The administration of ethanolic extract of mallaca leaves with repeated doses on mice did not have toxic effect on liver. It was assumed that Malacca leaves not adequate to affect the liver damage.

**CONCLUSION**

The administration of malacca leaves ethanolic extract with repeated doses for 21 days does not have negative effect on the liver of mice.

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Toxicity Subchronic Ethanolic Extract of Malaka (*Phyllanthus emblica*) Leaves


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