ACUTE TOXICITY TEST OF RAMBUTAN LEAF (*Nephelium lappaceum* L) EXTRACT IN MICE

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Abstract

Background. *Rambutan (**Nephelium lappaceum** L.) has been widely and easy to obtain, and also recognized by people of Indonesia. As empirically, rambutan leaves used to treat diarrhea, fever, and black hair. The preclinical studies have shown that rambutan leaf extract has activity as lowering blood glucose levels (Kusuma, 2008). However, the scientific studies have not found rambutan leaf safety. To be eligible in the formal health care system, it must meet the requirements of traditional medicine quality, safety, and efficacy.*

Objectives. *This study aimed to test the acute toxicity of rambutan leaf extract in mice. The study followed unidirectional random pattern.*

Methods. *The study use 25 Swiss Albino male of mice, which is divided into 5 dose groups. The dose used in the acute toxicity test of rambutan leaf extract are 1, 2, 4; 8 g/kgBBmice and a negative control group (0.5% CMC-Na) as orally. The inspection do the 24-hour by intensive inspection on the first 3 hours.*

Outcome Measured. *The observations made as clinical observations that toxic symptoms occur, the number of dead mice and biochemical examination of ALT levels, AST, and serum creatinine. The LD_{50} calculations performed using the Thompson-Weil.*

Results. *The results showed toxic symptoms were observed in mice during acute toxicity test include uncontrollable way, restlessness, passivity motion, no reactivity to stimuli, and sleepy. The test compound caused a significant increase in ALT and AST levels ($p < 0.05$) at a dose of 8 g/kgBB, but the test compound did not cause death in test animals.*

Conclusion. *The test compound can be categorized as "Practice Not Toxic".*

Keywords : *toxicity, extract, rambutan, Nephelium*

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ISBN : 978-979-18458-6-1

INTRODUCTION

In recent years, due to side effects of synthetic products, herbal medicine are gaining popularity in the world, particularly plant drugs for their primary healthcare. That is documented that 80% of the words population has faith in herbal medicine (Dubey *et al.*, 2004). Rambutan leaf (*Nephelium lappaceum* L) has been widely recognized by Indonesia people to treat various of diseases. As empirically, rambutan leaf has been used to treat diarrhea, fever and black hair (Dalimartha, 2004). The preclinical studies have shown that rambutan leaf extract have antimicrobial activity, antioxidant, and antiatheroschlerosis (Mohamed *et al,* 1994; Istikharah, 2007; Singhatong et al., 2010). Another studies have been conducted by Kusuma (2008) and Manaharan (2012) suggests that rambutan leaf has activity as lowering blood glucose in mice. Rambutan leaf has been suggested as source of potential useful antidiabetic drugs. However the toxicity of rambutan leaf has not been extensively studied. The numerous warnings regarding the potential toxicity of these therapies is needed for practitioners to keep abreast of the reported incidence of hepatotoxicity, nephrotoxic and cardiotoxic caused by the ingestion of herbal medicine (Saad *et al.*, 2006). This effort is very important that could be used rambutan leaf as standardized herbs that has been tested the efficacy and the safety.

Objectives

The general objective of this study was to determine the toxicity level of rambutan leaf (*Nephelium lappceum* L) extract in mice. Spesific objective is to determine the acute toxicity value (LD50) of rambutan leaf (*Nephelium lappaceum* L) extract in mice.

METHODS

Plant Material

Rambutan leaf were collected at Ngluwar Muntilan, Indonesia and were authenticated at Pharmacy Biological Laboratory, Islamic University of Indonesia based on Flora of Java book (Backer and Van der Brink, 1965). Powdered leaf of Rambutan (145 g) was macerated of ethanolic 70% at room temperature for 1 day and continued was percolated for 3 days. The resulting extract was concentrated to dryness to obtain a mass of ethanol extract (29.3 g) with the extraction yield of (20.21%).

Animals

The experimental animals used in this study were 25 Swiss Albino mice of male sexes each weighing 20-30 g and aged 8-10 weeks (Tedong, *et al.*, 2007). All animals were available at Integrated Research and Testing Laboratories, Gadjah Mada University. The animals were randomly distributed into five groups. All animals (mice) were maintained at constant temperature and humidity.

Acute Toxicity

In order to study any possible toxic effect or changes in normal behaviour, four groups of 5 mice were used in this experiment. The acute toxicity of the plant was studied by preparing four different concentrations of the extract (1.0, 2.0, 4.0, 8.0 g/Kg body weight) respectively was administered orally, to the animals as a single dose. The control group was given diluted solution in water. The symptoms of toxicity such as motor activity were cheked on the first 3 hours (Tedong *et al.*, 2007). The animals were observed for 24 hours and the number of dead mice was recorded and used in the calculation of the acute toxicity value (LD50).

Statistical Analysis

Statistical analysis was carried out using One-Way Analysis of Variance (ANOVA) continued Kruskal-Willis test. P values of less than 5% ($P < 0.05$) was considered statistically significant differences between the groups (Tedong *et al.,* 2007).

RESULTS

In this study, there were no mortality (expressed as LD50) after oral administration of single doses of rambutan leaf up to 8 g/kg (Table 1). However, the biochemical parameter (ALT, AST) increased progressively with increasing dose (Table 2). The reduction of motor activity (uncontrollable way, restlessness, passivity motion, no reactivity to stimuli, and sleepy) were seen since at dose of 1 g/kg up to a dose of 8 g/kg.

DISCUSSION

Acute treatment of the mice with rambutan leaf extract at doses of 1.0, 2.0, 4.0 g/kg for 24 hours did not affect biochemical parameters. On the other hand, administration of rambutan leaf extract at dose of 8 g/kg for 24 hours resulted in significant changes in the levels of transaminases (ALT, AST), and creatinine. There were good indicators of liver and kidney functions (Tedong *et al.*, 2007). It is reasonable to deduce that the rambutan leaf extract induce damage to liver and kidneys. The changes in the biochemical parameter has been studied by Tedong *et al.* (2007) and Mohammed *et al.* (2012) by histopathological examination of selected organs showed liver infiltration and congestion, kidneys' mesangial expansion and nucleus pycnosis. Histopatological indicated mild vascular degenerative changes and necroses to liver and kidney when compared to that of control group. The change biochemical parameters of rambutan leaf extract may be related to its tannin content. Importanly, so many species which contain tannin have been shown to display a wide spectrum of toxicological activities. Diets tannin had deleterious effects on liver of the rabbits and rats (Obidah *et al*., 2010; Fayemi *et al*., 2011).

The ethanolic rambutan leaf extract (1, 2, 4, 8 g/kg) produced a reduction in spontaneous motor activity, motor coordination, sleepy and depressant. Preliminary qualitative chemical studies of some plants indicated tannin in the extract suggested that contains some active

Table I. Acute Toxicity of Rambutan leaf (*Nephelium lappaceum* L) extract in mice

Number of mice	Dose of extract g/kg	Number of mice dead	Percentage of mice dead
5	0.0	0	0
5	1.0	0	0
5	2.0	0	0
5	4.0	0	0
5	8.0	0	0

Table II. Biochemical Animal Test After 24 hours administration

Dose of extract g/kg	*SGPT (u/l)*	*SGOT (u/l)*	Kreatinin (mg/dl)
0.0	*56.0*	*111*	0.3
1.0	*49.5*	*93.5*	0.2
2.0	*49.0*	*81*	0.4
4.0	55.0	105.5	0.3
8.0	122.0	227.0	0.2

principles which possess potential CNS-depressant action, decreased loco-motor activity, produced muscle relaxation and showed antianxiety activity (Bhosale et al., 2011; Habib et al., 2011; Raju *et al.*, 2011).

In this study, there was no lethality observed for all the tested doses throughout the 24 hours period as well as tannins at *Cinnomomum iners* leaves was no lethality (Mustaffa *et al*., 2010).

CONCLUSION

On the basis of present study, it can be concluded that rambutan leaf extract appears to be free from acute toxicity and relatively safe within the normal doses. However it is recommended for the next studies:

a) To determine histologically the acute toxicity effects of rambutan leaf the internal organs of mice

b) Acute toxicity test used more various dose and more obeserved day .

c) Sub-acute and chronic toxicity tests is planned in order to determine the long-term effects of the extract.

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