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Analysis of Body Weight Profile and Signs of Acute Toxicity White Rats on Giving Ethanol Fraction of Rambutan Peel (*Nephelium lappaceum* L)

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ABSTRACT

Introdiction: Rambutan peel (*Nephelium lappaceum* L) contains antioxidant compounds like flavonoids such as anthocyanins. The high antioxidant activity causes the high utilization of rambutan peel for treatment, but its side effects on the body are unknown. **Aims**: This study aimed to analyze the effect of giving rambutan rind ethanol fraction on body weight and toxic symptoms in white rats. **Methods**: The test was carried out using the OECD 425 method in which there were three treatment groups, each consisting of 5 test animals that were given the preparation orally. Treatment 1 was only given 1% CMC Na for 14 days; treatment 2 was given the ethanol fraction of rambutan peel 400 mg/200 g BW which was observed every 30 minutes for 4 hours, then up to 48 hours, then every day for up to 14 days. If there is none, it is continued with treatment 3, which is given the ethanol fraction of rambutan peel 1000 mg/200 g BW for 14 days. Symptoms of acute animal toxicity were observed for 14 days in that treatment. **Result:** The results showed that the ethanol fraction of rambutan peel doses of 400 mg/200 g BW and 1000 mg/200 g BW had a significant effect (p=0.017) in increasing the body weight profile of white rats, and there were no signs of acute toxicity in each treatment group. **Conclusion:** The dose of the ethanol fraction of rambutan peel 400 mg/200 g BW is the best, with an increased body weight of 25.17%.

KEYWORDS: Rambutan peel ethanol fraction, antioxidant, body weight, signs of acute toxicity, OECD 425.

INTRODUCTION

Plants used in traditional medicine must meet several requirements, including quality, safety, and nature. Pre-clinical tests are required, one of which is toxicity testing, when the first step is acute toxicity at one dose within 2 hours (BPOM, 2014). One of the traditional medicinal plants that have many activities is rambutan peel. Rambutan is a plant widely cultivated in Indonesia for its fruit, while the red peel of the rambutan fruit is a waste and needs to be used optimally (Wardhani, 2015). Rambutan peel contains many secondary metabolites such as steroids, terpenoids, tannins in the form of allergic acids, phenolics, and the highest flavonoids in the form of anthocyanin compounds such as geranin and corilagin (Wulandari, 2012).

Anthocyanins are organic compounds from the flavonoid group which also act as antioxidants (Faramayuda, 2022). Antioxidants are compounds that have an imp-

ortant role in protecting body cells from damage (Putri, 2019). The antioxidant activity of anthocyanin compounds works by capturing free radicals and increasing the regulation of intra-cell antioxidant enzymes (Kurniasari, 2022). Based on research, rambutan peel contains anthocyanins which act as antioxidants (Setyani, 2022).

Fractionation is carried out using the liquid-liquid fractionation method, in which the compounds contained in the extract are separated according to the properties of the liquid solvent. The purpose of fractionation is to separate compounds based on polarity from crude extracts into simpler fractions to facilitate the isolation of the target compound. In this study, fractionation was carried out from the ethanol extract of rambutan peel to attract polar active compounds such as flavonoids into the ethanol fraction. (Daiyanti, 2023). Therefore, a toxicity test must be carried out to assess the safety of the ethanol fraction of rambutan peel. This study aims to analyze the effect of the ethanol fraction of rambutan peel on white rats' body weight and signs of acute toxicity. The toxicity test carried out in this study was an acute oral toxicity test. Acute toxicity using the OECD (Organization for Economic Cooperation and Development) 425 is a measurement development method from the scope of the LD50 value on behavioral observations, psychological activity, body weight, macro organs, or agency index (OECD, 2008).

MATERIAL AND METHODS

Material

The tools used for extraction and fractionation are macerators, analytical balances (*Shimadzu AUY-220*), rotary vacuum evaporators (*Eyela*), centrifuges (*LC-04S*), separating funnels (*Pyrex*), and other glassware. Tools for the toxicity test are oral probes, syringes, animal jars, animal cages, animal scales, and wire rams. The materials used in this study were rambutan skin, white rats, standard feed, 1% Na CMC (*bratachem*), NaOH (*bratachem*), HCl (*bratachem*), 96% ethanol (*Merck*), chloroform (*Merck*), ethyl acetate (*Merck*) and aqua dest.

Method

Selection and Handling of Test Animals

The testing procedure in this study was reported to the Bakti Tunas Husada University with Ethics Commission with No.054/ec.02/kepk-bth/VI/2022. White rats, weighing 150-200 g, used in this study were maintained at room temperature and acclimatized. Rats are given standard feed and drink enough water; five mice were used for each treatment.

Fraction Preparation

1000 grams of rambutan peel powder was weighed into a 1 L Erlenmeyer, added ethanol solvent: 1% HCl (10:1) until all the simplicial was submerged until a clear extract was produced. The filtrate obtained was then concentrated using a rotary evaporator. The

viscous extract obtained was weighed using an analytical balance, and the yield was calculated. N-hexane was added to the condensed extract, shaking it several times using an orbital shaker until the color of the n-hexane solution was clear. Add ethanol to the residue and shake again with an orbital shaker until the ethanol solution is clear. Collect the ethanol fraction and calculate % yield of the fraction obtained (Alina, 2020)

Anthocyanin Qualitative Test

Simplisia of rambutan peel was reacted with 2M HCl and then heated at 100°C for 5 minutes. Then 2M NaOH was added drop by drop while observing the change. Do the same procedure for extracts and fractions (Faramayuda, 2022)

Analysis of Signs of acute toxicity

Analysis of symptoms of acute toxicity was carried out using *the up-down procedure* OECD 425. Five rats were fasted for 3-4 hours before administering the ethanol fraction of the rambutan peel. The test was carried out using the OECD 425 method in which there were three treatment groups, each consisting of 5 test animals that were given the preparation orally. Treatment 1 was only given 1% CMC Na for 14 days; treatment 2 was given the ethanol fraction of rambutan peel 400 mg/200 g BW which was observed every 30 minutes for 4 hours, then up to 48 hours, then every day for up to 14 days. If there is none, it is continued with treatment 3, which is given the ethanol fraction of rambutan peel 1000 mg/200 g BW for 14 days. Symptoms of acute animal

Analysis of body weight profile and signs toxicity were observed for 14 days in that treatment (OECD, 2008).

Observation of Body Weight of Mice

All rat test animals were weighed on day 0 before administration of the extract, then on days 4, 7, 10, and 14 after administration of the ethanol fraction of rambutan peel. An increase or decrease in body weight is recorded, observed, and analyzed (OECD, 2008).

Observation Of Signs of acute toxicity

Observations were made for 14 days after being administered orally in all treatments. Observations were made by observing symptoms in the form of signs of toxicity such as peel and fur, eyes, lethargy (lethargy), convulsions (seizures), tremors (shaking), diarrhea, and death (OECD, 2008).

Data Analysis

Data are reported as the mean ± standard error of the mean (SEM). Data analysis was performed by one-way analysis of variance (ANOVA) followed by a statistical LSD and Duncan posthoc test (Nurfaat, 2016).

RESULTS AND DISCUSSION

Rambutan peel is extracted by maceration because the red dye on rambutan peel is not heat resistant. Maceration was carried out with 1% ethanol: HCl (10:1) solvent, which aims to break the glycosidic bonds in the anthocyanin compounds. The yield of the thick extract obtained was 57.85%. The anthocyanin contained in the rambutan peel fraction is in the ethanol fraction because anthocyanins are

Table 1. Anthocyanin content in rambutan peel

Reagent	Simplisia	Extract	Fraction	Result
HCl 0.1 N	+	++	++	Dark red
NaOH 0.1 N	+	++	++	Dark green

Information :
+: weakly detectable anthocyanins
++: Strong detectable anthocyanins

flavonoid compounds that dissolve in water and ethanol (Nurfadillah, 2016). A qualitative test of anthocyanins on rambutan peel found that the highest anthocyanin content was found in extracts and fractions, which indicated a change in the color of the sample to dark red when added with HCl and turned dark green when added with NaOH. The ethanol fraction of rambutan peel is the most concentrated, which indicates that anthocyanin is attracted to ethanol, so the highest anthocyanin content is in the ethanol fraction (Table 1).

Based on the observations in Table 2, the body weight of the rats given the rambutan peel ethanol fraction at doses of 400 mg/200 g BW and 1000 mg/200 g BW experienced the most increase in body weight compared to normal controls. However, the increase in body weight was the highest, namely the ethanol fraction of rambutan peel dose of 400 mg/200 g BW. This shows that the ethanol fraction of rambutan peel can increase the appetite of rats so that they experience an increase in body weight.

Based on the results of statistical analysis, data normally distributed with a value of p=0.099 (p>0.05) and homogeneous with a value of p=0.696 (p>0.05). The results of the ANOVA test analysis showed that there was a significant difference between the treatment groups with a value of p=0.017 (p>0.05), where based on the results of the LSD test, there was a significant difference between normal controls with a dose of 400 mg/200 g BW and an increase in body weight The largest was the ethanol fraction of rambutan peel 400 mg/200 g BW based on the Dunchan test. The increase in body weight of rats showed that the ethanol fraction of rambutan peel doses of 400 mg/200 g BW and 1000 mg/200 g BW were not toxic but increased the growth of rats.

Based on the calculation results, the highest proportion of body weight increase was the ethanol fraction of rambutan rind at a dose of 400 mg/200 g BW. The increase in weight in the group given the fraction could be interpreted as a good physical condition. There was stimulation of appetite and drinking from the compound content of the ethanol fraction of rambutan peel accompanied by active physical activity (Muniroh, 2013).

In the 4 hours of observation of fraction administration, there were no changes in qualitative parameters such as peel and hair changes, mucous membranes, respiratory system, eyes, autonomic nervous system, circulatory system, behavior pattern, and somatomotor (tremors, convulsions, paralysis, and coma) (Sulastra, 2020). After 24 hours of observation, there was no signs of acute

Table 2. Observation results of rat body weight

Treatment Group	Body Weight (gram) ± SD				
	Day 0	Day 4	Day 7	Day 10	Day 14
Normal control	162.4±13.9	163.4±11.5	152.8±11.3	151.2±8.0	155.6±8.5
Ethanol fraction 400 mg/200 g BW	145.4±2.2	151.4±7.6	143.8±7.7	169.4±13.5	182±10.8
Ethanol fraction 1000 mg/200 g BW	155.4±4.8	158.6±5.8	147±5.2	161.6±8.8	171.2±12.4

toxicity, and no death occurred. Based on the results of observations for 14 days, there were no deaths and changes in the qualitative toxicity parameters in the 3 test groups. This indicates that the ethanol fraction of rambutan peel is not toxic because it does not show signs of toxicity.

CONCLUSION

The results showed that the ethanol fraction of rambutan peel doses of 400 mg/200 g BW and 1000 mg/200 g BW had a significant effect (p=0.017) in increasing the body weight profile of white rats, and there were no signs of acute toxicity in each treatment group. The dose of the ethanol fraction of rambutan peel 400 mg/200 g BW is the best, with an increased body weight of 25.17%. It is necessary to carry out a subchronic toxicity test to determine the long-term effect of giving the ethanol fraction of rambutan peel.

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