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Hepatoprotector Effect of Banana Peel (*Musa paradisiaca Sapientum*) on Paracetamol Induced Rats

(*Efek Hepatoprotektor Kulit Pisang Raja* (*Musa paradisiaca Sapientum*) *pada Tikus Yang Diinduksi Parasetamol*)

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ABSTRACT

Background: Liver disease is still a disease with high prevalence in Indonesia. One of drug-induced liver injury is paracetamol. Banana peel (*Musa paradisiaca Sapientum*) has flavonoid compounds that could increasing the production of glutathione enzymes in the liver. **Objectives:** This research aims to determine the hepatoprotector activity of banana peel methanol extract on rats induced by paracetamol. **Material and Methods:** This research is an experimental with pre and post test control group design method. Group I was given 0.05% Na CMC as negative control, group II was given paracetamol 180 mg/kgBB as induction control group, group III was given banana peel extract at dose 700 mg / kg BW, group IV was given banana peel extract at dose 1400 mg/kg BW, and group V was given banana peel extract at dose 2100 mg/kg BW. **Results:** The liver damage determined by measuring SGOT/SGPT serum levels of rats. The liver damage determined by measuring SGOT/SGPT serum levels of rats. The SGOT post-test levels of banana peels with dose 700 mg/kg BW, 1400 mg/kg BW and 2100 mg/kg BW were consecutively 69.20 UI/L, 73.29 UI/L and 73.80 UI/L. The SGPT levels post-test of banana peels with dose 700 mg/kg BW, 1400 mg/kg BW and 2100 mg/kg BW were consecutively 41.00 UI/L, 33.80 UI/L, and 51.29 UI/L. The SGOT and SGPT post-test levels of banana peels is lower than SGOT and SGPT pre-test levels. Statistical data analysis with paired sample T test obtained the value of p = 0.003 for SGOT (serum glutamic oxaloacetic transaminase) and p = 0.000 for SGPT. **Conclusions:** Both SGOT and SGPT values have p <0.05 which indicates that banana peel (*Musa paradisiaca Sapientum*) methanol extract has significantly hepatoprotector effect on paracetamol-induced rats.

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ABSTRAK

Latar Belakang: Penyakit hati merupakan penyakit yang prevalensinya masih tinggi di Indonesia. Salah satu obat yang dapat menyebabkan kerusakan pada hati adalah parasetamol. Kulit pisang raja (*Musa paradisiaca Sapientum*) mengandung senyawa flavonoid yang dapat meningkatkan produksi enzim glutation pada hati. Tujuan: Penelitian ini untuk mengetahui efek hepatoprotektor ekstrak metanol kulit pisang raja pada tikus yang diinduksi parasetamol. Bahan dan Metode: Penelitian ini merupakan penelitian eksprimental dengan design *penelitian pre and post-test control group*. Hasil: Kerusakan hati ditentukan melalui pengukuran kadar SGOT/SGPT serum tikus. Nilai konsentrasi SGOT kulit pisang raja dengan dosis 700 mg/kg BB, 1400 mg/kg BB dan 2100 mg/kg BB pada saat post-test berturut-turut adalah 69,20 UI/L, 73,29 UI/L dan 73,80 UI/L. Nilai konsentrasi SGOT kulit pisang raja dengan dosis 700 mg/kg BB, 1400 mg/kg BB dan 2100 mg/kg BB pada saat *post-test* berturut-turut adalah 41,00 UI/L, 33,80 UI/L, dan 51,29 UI/L. Nilai konsentrasi SGOT dan SGPT kulit pisang rasa pada saat *post-test* lebih rendah dibandingkan dengan nilai konsentrasi SGOT dan SGPT pada saat *pre-test*. Data dianalisis menggunakan SPSS dengan uji ANOVA *Paired sample* T *test* dengan hasil yang diperoleh p=0,003<0,05 untuk kadar SGOT dan P=0,000<0,05 untuk kadar SGPT. Kesimpulan: Kadar SGOT dan SGPT dengan nilai p<0,05 yang mengindikasikan bahwa ekstrak metanol kulit pisang raja (*Musa paradisiaca Sapientum*) memiliki efek hepatoprotektor yang berbeda signifikan terhadap tikus yang diinduksi parasetamol .

Kata kunci: Kulit pisang raja, hepatoprotektor, SGOT, SGPT.

INTRODUCTION

Liver disease is still high prevalence in Indonesia. Liver damage was associated with the dysfunction due to exposure to drugs or other noninfectious agents that called hepatotoxicity (Fisher et al., 2015; Roy et al., 2012). One of the caused hepatotoxicity by using hepatotoxic drugs. Drug-induced liver damage results when the liver is unable to detoxify the free radicals or other toxic metabolites from drug substances. Most acute liver disease occurring due to overdose of acetaminophen (N-acetyl-p-aminophenol, paracetamol, APAP). APAP is a drug to relive fever and pain used worldwide and prescribed or non-prescribed in other drugs (Ghanem et al., 2016); Shiffman et al., 2018; Ishitsuka et al., 2020). Drug inducing liver disorders were caused by 37% of paracetamol toxic dose (Pandit et al., 2012). Acetaminophen is a drug as safe at normal doses (Piotrowska et al., 2019). Several of data reported morbidity intoxication of APAP (Pholmoo and Bunchorntavakul, 2019; Rubin et al., 2018). Hepatotoxicity of paracetamol may occur in a single dose of 10-15 grams every 4-6 hours up to a maximum daily dose of 50-75 mg/kg (Lancaster et al., 2015). Adverse events related with paracetamol toxicity are acute liver failure (ALF), centrilobular hepatic necrosis, renal tubular necrosis and hypoglycaemic coma (Lancaster et al., 2015; De-Giorgio et al., 2013; Rafita et al., 2015). Metabolism of paracetamol is in liver microsomes, a few percentages of paracetamol (5-10%) is converting by cytochrome P450 isoforms (CYP2E1, CYP2A6) into a reactive metabolite, N-acetyl-para-benzo-quinone imine (NAPQI), most of the related to paracetamol hepatotoxicity (McGill and Jaeschke, 2013; Mazaleuskaya et al., 2015).

Hepatotoxicity can be prevented by hepatoprotectors agent (Roy et al., 2012). Banana is one of the plants that has potency as hepatoprotector. Waste of banana peel in the world is high and it is less utilization (Sivaranjana and Arumugaprabu, 2021). Banana peel have an antimicrobial effect and antioxidant activity (Chabuck et al., 2013; Kapadia et al., 2015). It contains antioxidant compounds, including phenolic, flavonoids, terpenoids, polyphenols and tannins (Singhal and Ratra, 2013; Pusmarani et al., 2019). Fruits of banana peel (*Musa Sapientum*) possesses hepatoprotective potential (Issa et al., 2018). Banana peel contains flavonoid that can decrease lipid peroxides and increase glutation enzyme on heart (Boadi et al., 2021). Research on banana peel activity as hepatoprotector has not been done yet, so it is necessary to do the research to know the effect of banana peel extract as hepatoprotector on paracetamol-induced rats.

MATERIAL AND METHODS

Materials

The materials used in this research were aqua distillata, methanol, Na CMC, cotton, filter paper and banana peel (*Musa paradisiaca Sapientum*). The ripe banana was collected from the Bombana, Southeast Sulawesi. The test animals were male Wistar rats aged 2-3 months with an average body weight of 200-300 grams. The rats were obtained from LPPT, Gadjah Mada University, Yogyakarta. This study was carried out in accordance with the Guide for the Care and Use of Laboratory Animals (National Research Council (US) Committee, 2011) and an experimental protocol approved by the research ethics committee at Halu Oleo University with the number 2685/UN29.20/PPM/EC/2018.

Methods

Extraction

In this research, banana peel (3 kg) was extracted by maseration method at room temperature with methanol solvent as much as 5 L for 24 hours and repeated as much as 3x for 5 days. Once filtered with filter paper, the obtained filtrate was evaporated on the rotary evaporator until reached a little thick extract. Then the evaporation was continued on a stainless-steel pan above the water heater until a thick extract was obtained. Then the extract was weight and rendement was calculated.

Experimental

This research is experimental laboratory with pre-test and post-test control group design. It conducted at Pharmacology Laboratory of department Pharmacy of Universitas Mandala Waluya and Integrated Clinical Laboratory of Health Analyst of Mandala Waluya University. The rats were adapted to the laboratory environment for 10 days and divided randomly into 5 groups with each group consist of 5 test animals, feeding was standard feed and ad libitum. Group 1 was a negative control group given NaCMC 0.05%. Group 2 was given paracetamol 180 mg/kg BW as induction control group. Group 3,

4, and 5 were treated with methanol extract of banana peel at dose 700 mg/kg BW, 1400 mg/kg BW and 2100 mg/kg BW. On the 1st day, before the treatment, blood sampling and SGOT (serum glutamic oxaloacetic transaminase) and SGPT (serum glutamic pyruvic transaminase) counting levels were done in each group. Methanol extract of banana peel was given for 7 days. On the 8th day, paracetamol induction of 180 mg/kg BW was given to group 3, 4, and 5. On the 9th day, blood samples were collected on all test animals and SGOT and SGPT levels were examined. Determination of SGPT and SGOT blood serum activity was performed on the test animals before giving paracetamol and the eighth day. The obtained serum (0.1 ml) was mixed with SGPT or SGOT (1.0 ml) reagent which was preheated at 37°C. The serum and reagent mixture were incorporated into the MINRAI 88 Spectrophotometer tool and measured its absorbance at 340 nm. The results of SGOT and SGPT activity were expressed in units of unit/liter (U/L) which was the number of enzymes in a liter of serum that could produce NAD^+ at the same time unit.

RESULTS AND DISCUSSION

Damage cells in the liver could be known by doing biochemical examination which is the measurement of SGOT and SGPT enzymes levels. SGPT and SGOT enzymes are enzymes that come out into the blood when the damage occurred in the liver cells (Victor, 2016; Fristiohady et al., 2020). The markers of liver damage is the increasing of SGOT or SGPT levels (Rosida, 2016). SGOT and SGPT enzymes are two enzyme that synthesized in liver. SGPT is an enzyme to had large amounts in liver. SGOT is an enzyme contained in the cystosol of liver hepatocytes, but also it is found in the heart, skeletal muscle, kidney, and brain (Vagvala and O'Connor, 2018). The result of SGOT levels measurement on group of 700 mg/kg BW, 1400 mg/kg BW, and 2100 mg/kg BW banana peel extract showed a decrease in SGOT levels after 7 days treatment as shown in Table 1.

Table 1. Effect of M*usa paradisiaca Sapientum* methanol extract on liver and SGOT levels in APAP-administrated on rats

Group	Mean (UI/L) ± SD	
	Pre-test	***Post-test***
Group 1 (Negative control)	161.20±32.33	129.40±30.71
Group 2 (180 mg/kg BW Paracetamol)	102.60±18.19	110.00±13.71
Group 3 (700 mg/kg BW Banana peel extract)	123.00±49.55	69.20±14.00*
Group 4 (1400 mg/kg BW Banana peel extract)	124.80±24.08	73.20±15.02*
Group 5 (2100 mg/kg BW Banana peel extract)	135.00±43.90	73.80±17.9*

* Indicates a decrease in SGOT levels after giving the treatment of banana peel extract with LSD test value is showed p values <0.05; SGOT, serum glutamate oxaloloacetate transaminase

Table 2. Effect of M*usa paradisiaca Sapientum* extract on liver and SGPT levels in APAP-administrated on rats

Group	Mean (UI/L) ± SD	
	Pretest	***Post Test***
Group 1 (Negative control)	50.60±36.65	61.20±36.87
Group 2 (180 mg/kg BW Paracetamol)	23.40±12.14	33.40±16.92
Group 3 (700 mg/kg BW Banana peel extract)	44.40±20.34	41.00±13.09*
Group 4 (1400 mg/kg BW Banana peel extract)	46.00±22.02	33.80±8.47*
Group 5 (2100 mg/kg BW Banana peel extract)	51.20±19.92	47.00±15.65*

* Indicates a decrease in SGPT levels after giving the treatment of banana peel extract with LSD test value is showed p values <0.05; SGPT, serum glutamate pyruravate tansaminase

The obtained data were then tested statistically by using ANOVA Paired sample T test to determine if there was any difference before and after the treatment. The results were p = 0.003 for SGOT and p = 0.000 for SGPT. Of these two values, p <0.05 indicates that banana peel methanol extract could significantly decrease the SGOT and SGPT levels of rat blood serum. Similar to another results that flour of banana peel has a hepatopeotective effect in diabetic-rats by mechanism of controlling hepatic enzyme transaminase and inducing liver regeneration (Nurrahma et al., 2021).

Paracetamol is one of the drugs that can cause hepatotoxicity if used in excessive doses (McGill and Jaeschke, 2013). The hepatotoxic mechanism of paracetamol was caused by damage of liver cell which is resulted from metabolites formed during reaction with cytochrome P450. The main metabolical pathway of therapeutic paracetamol dose is through glucoronidation and sulfotation in the liver, and only a few of the doses could produce N-acetyl-p-benzoquinone (NAPQI) derived from the metabolic product of oxidation by cytochrome P450. NAPQI has ability binding the sulfhydryl groups on cysteine and lysine residues of the hepatocytes mitochondrial proteins that results the defisiency of the mitochondrial respiration, the enhance of stress oxidative and dysfunction with ATP stores elimination in mitochondrial. NAPQI compounds is from free radical toxic protein that damaged to rat liver cells (Wang et al., 2017). Another hepatotoxicity mechanism of paracetamol includes the formation of peroxynitrite, a toxic free radical produced in the mitochondria, from a superoxide and nitric oxide reaction by causing oxidative injuries (Yoon et al., 2016).

Hepatotoxicity could be prevented by giving hepatoprotective drugs (Mishra et al., 2014). It is a compound that could protect liver cells against toxic substances that damage these cells. Antioxidant compounds such as flavonoid and phenol could serve as hepatoprotectors (Rahardian et al., 2010). Yellow ripe banana peel is rich in flavonoids, phenol, saponin, terpenoids and tannins compounds which are antioxidants of liver disease so banana peel could work as hepatoprotectors (Ehiowemwenguan et al., 2014; Pusmarani et al., 2020). The mechanism of flavonoids as hepatoprotector is through the detoxification process by increasing the expression of Gluthation S-Transferase (GST) enzyme, which is an endogenous antioxidant in the liver. GST enzymes serve to detoxify by converting less polar

substances to more polar through the binding of active electron which is unpaired to toxic substances (Boušová and Skálová, 2012). Banana peel (*Musa paradisiaca Sapientum*) have hepatoprotector effect against paracetamol-induced on rats.

CONCLUSION

Methanolic extract of banana peel (*Musa paradisiaca sapientum*) at dose 700 mg/kg BW, 400 mg/kg BW and 2100 mg/kg BW could be a hepatoprotector because it can decrease the SGOT and SGPT serum levels of rats.

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CONFLICT OF INTEREST

Authors declares no conflict of interest

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