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Hepatoprotective Effect of Ethanol Extract of Kepok Banana Peels (Musa paradisiaca) on Cisplatin-Induced Hepatotoxicity in Rats

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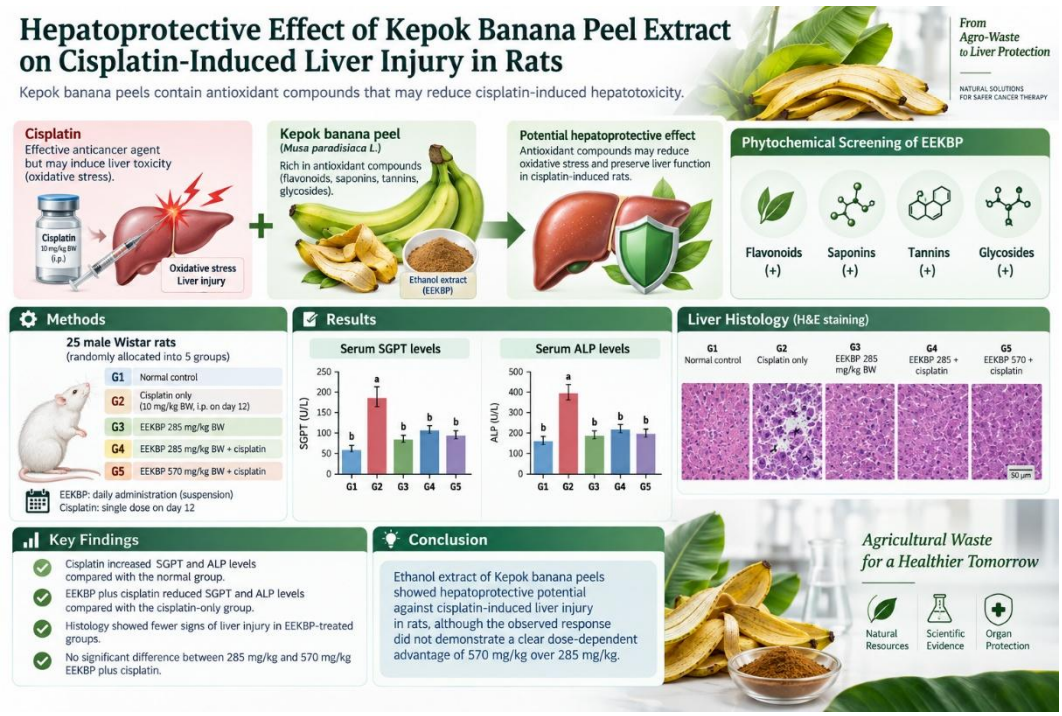
Graphical Abstract



Abstract: Background: Cisplatin is an effective antineoplastic agent, but its clinical use is limited by organ toxicity, including liver injury associated with oxidative stress. Kepok banana peel contains antioxidant compounds that may reduce cisplatin-induced hepatotoxicity. Objective: This study evaluated the hepatoprotective effect of ethanol extract of Kepok banana peels (EEKBP) in cisplatin-induced rats. Methods: Twenty-five male Wistar rats were randomly allocated into five groups: normal control, cisplatin only, EEKBP 285 mg/kg body weight, EEKBP 285 mg/kg body weight plus cisplatin, and EEKBP 570 mg/kg body weight plus cisplatin. Cisplatin was administered intraperitoneally at 10 mg/kg body weight on day 12, and EEKBP suspension was administered daily according to group allocation. Serum glutamic pyruvate transaminase (SGPT), alkaline phosphatase (ALP), phytochemical screening, and liver histology were assessed. Results: Phytochemical screening showed flavonoids, saponins, tannins, and glycosides in EEKBP. Cisplatin increased mean SGPT and ALP levels compared with the normal group. Rats receiving EEKBP plus cisplatin had lower SGPT and ALP levels than the cisplatin-only group, and histology showed fewer qualitative signs of liver injury. The 285 mg/kg and 570 mg/kg EEKBP plus cisplatin groups did not differ significantly from each other. Conclusion: EEKBP showed hepatoprotective potential against cisplatin-induced liver injury in rats,

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although the observed response did not demonstrate a clear dose-dependent advantage of 570 mg/kg over 285 mg/kg.

Keywords: alkaline phosphatase; cisplatin; ethanol extract; hepatoprotective; Musa paradisiaca; serum glutamic pyruvate transaminase

INTRODUCTION

Cancer remains a major global cause of morbidity and mortality, and chemotherapy continues to be central to treatment for many solid tumors.[1] Cisplatin, a platinum-based antineoplastic agent, is widely used in lung, ovarian, testicular, kidney, head and neck, and other cancers. Its therapeutic benefit is limited by toxicity in several organs, including the liver, kidney, nervous system, and inner ear.[2,3]

Cisplatin-induced hepatotoxicity is multifactorial. Experimental studies suggest that oxidative stress, reactive oxygen species, lipid peroxidation, glutathione depletion, inflammatory-cell infiltration, hepatocyte degeneration, and apoptosis contribute to liver injury.[2-5] Because oxidative stress is a major pathway in this process, antioxidant-rich plant extracts have been evaluated as possible protective agents. Ginger extract, curcumin, and alpha-tocopherol have shown protective effects against cisplatin-related liver injury in rat models.[6,7]

Kepok banana (Musa paradisiaca) is used in traditional medicine, and banana peels contain secondary metabolites such as flavonoids, tannins, saponins, and other antioxidant compounds.[8-11] Previous studies have reported antioxidant activity and effects of banana peel extracts on biochemical parameters related to liver function.[10,11,13] However, evidence on the hepatoprotective potential of ethanol extract of Kepok banana peels against cisplatin-induced liver injury remains limited. This study aimed to evaluate whether EEKBP could improve serum liver-enzyme markers and liver histology in cisplatin-induced rats.

MATERIALS AND METHOD

Study design and setting

This experimental study used a completely randomized design. The research was conducted from July to September 2022 at the Pharmacology Laboratory, Faculty of Pharmacy, University of North Sumatra, and AA Main Clinic, Medan, Indonesia.

Experimental animals and grouping

Twenty-five male Wistar rats (Rattus norvegicus) with an initial body weight of approximately 200 g +/- 10% were allocated into five groups, with five rats in each group. Group A was the normal control. Group B received cisplatin only. Group C received EEKBP 285 mg/kg body weight only. Group D received EEKBP 285 mg/kg body weight plus cisplatin. Group E received EEKBP 570 mg/kg body weight plus cisplatin.

Preparation of Kepok banana peel extract

Kepok banana peels were purchased from a market in Medan, and plant determination was conducted at the Faculty of Mathematics and Natural Sciences, University of North Sumatra. Approximately 500 g of dried and powdered banana peel was macerated with 96% ethanol at a 1:3 w/v ratio and stirred at 250 rpm for two days. The mixture was filtered repeatedly to obtain a clear viscous filtrate. The extract was concentrated at 45-50 degrees Celsius using a rotary evaporator, and remaining solvent was evaporated using a water bath. Qualitative phytochemical tests were performed for flavonoids, tannins, steroids or triterpenoids, terpenoids, alkaloids, saponins, and glycosides using routine procedures.[7,11,12]

Cisplatin induction and sample collection

Cisplatin-induced hepatotoxicity was produced by intraperitoneal injection of cisplatin 10 mg/kg body weight on day 12, followed by monitoring until day 14. EEKBP suspension was administered daily according to group allocation. On day 15, animals were fasted with access to water before euthanasia. Liver tissue was collected, coded

by group, and processed for histological examination. Peripheral blood was also collected on day 15, centrifuged for 10 minutes at 3000-4000 rpm, and the serum was stored at -4 degrees Celsius before SGPT and ALP measurement using commercial enzymatic reagent kits.[7,11,12]

Statistical analysis

Data were analyzed using SPSS. Results are presented as mean and standard deviation. Normality and homogeneity of variance were assessed before between-group comparisons. The submitted analysis used independent t-tests for reported pairwise comparisons among treatment groups, with $p < 0.05$ considered statistically significant. Because multiple pairwise tests were performed in a small animal experiment, the p-values should be interpreted cautiously.

RESULTS AND DISCUSSION

Phytochemical screening

Qualitative phytochemical screening showed that EEKBP contained flavonoids, saponins, tannins, and glycosides, whereas triterpenoids and alkaloids were not detected (Table 1). These findings are consistent with reports that banana peels contain antioxidant-related compounds, including phenolics and flavonoids.[10,13]

Table 1. Phytochemical content of ethanol extract of Kepok banana peels

No.	Phytochemical	Result
1	Flavonoids	Found (+)
2	Triterpenoids	Not found (-)
3	Alkaloids	Not found (-)
4	Saponins	Found (+)
5	Tannins	Found (+)
6	Glycosides	Found (+)

Serum SGPT and ALP profile

The blood-serum profile of all groups is shown in Table 2. The normal control group had mean SGPT and ALP levels of 41.20 +/- 3.70 U/L and 92.00 +/- 9.49 U/L, respectively. The highest mean SGPT and ALP levels were observed in the cisplatin-only group, at 91.80 +/- 2.86 U/L and 188.00 +/- 8.50 U/L. Groups receiving EEKBP plus cisplatin had lower SGPT and ALP levels than the cisplatin-only group, although their values remained higher than the normal control group.

Table 2. Blood-serum SGPT and ALP levels in rats with cisplatin-induced hepatotoxicity

No.	Treatment group	SGPT mean	SGPT SD	ALP mean	ALP SD
1	Group A	41.20	3.70	92.00	9.49
2	Group B	91.80	2.86	188.00	8.50
3	Group C	50.20	2.49	107.80	11.50
4	Group D	57.60	8.20	154.40	6.70
5	Group E	62.60	6.77	160.60	14.19

SGPT: serum glutamic pyruvate transaminase; ALP: alkaline phosphatase; SD: standard deviation. Group A: normal; Group B: cisplatin only; Group C: EEKBP 285 mg/kg body weight; Group D: EEKBP 285 mg/kg body weight plus cisplatin; Group E: EEKBP 570 mg/kg body weight plus cisplatin.

Table 3. Pairwise difference tests for SGPT and ALP

Comparison		SGPT difference +/- SE	SGPT p-value	ALP difference +/- SE	ALP p-value
Group A	Group B	-50.60 +/- 2.09	0.000*	-96.20 +/- 5.70	0.000*
Group A	Group C	-9.20 +/- 1.99	0.002*	-15.90 +/- 6.67	0.045*
Group A	Group D	-16.40 +/- 4.02	0.004*	-62.40 +/- 5.19	0.000*
Group A	Group E	-21.40 +/- 3.45	0.000*	-68.60 +/- 7.63	0.000*
Group B	Group C	41.60 +/- 1.70	0.000*	80.40 +/- 6.39	0.000*
Group B	Group D	34.20 +/- 3.89	0.000*	33.80 +/- 4.84	0.000*
Group B	Group E	29.20 +/- 3.29	0.000*	27.60 +/- 7.40	0.006*
Group C	Group D	-7.40 +/- 3.83	0.090	-46.60 +/- 5.95	0.000*
Group C	Group E	-12.40 +/- 3.22	0.005*	-52.80 +/- 8.17	0.000*
Group D	Group E	-5.00 +/- 4.76	0.324	-6.20 +/- 7.02	0.403

*SE: standard error; *statistically significant at p < 0.05.*

Pairwise comparisons are presented in Table 3. Cisplatin only differed significantly from the normal control for both SGPT and ALP. SGPT and ALP levels in Groups D and E were also significantly lower than in the cisplatin-only group. However,

Group D and Group E did not differ significantly from each other for SGPT or ALP. The data therefore support a hepatoprotective effect of EEKBP against cisplatin injury, but they do not show that 570 mg/kg body weight produced a superior response compared with 285 mg/kg body weight.

Interpretation of liver-enzyme findings

Elevation of SGPT reflects hepatocellular injury and release of intracellular enzymes into the blood. Cisplatin-related oxidative stress can promote lipid peroxidation, glutathione depletion, apoptosis, and structural injury in hepatocytes.[2-5,14] The lower SGPT and ALP levels in the EEKBP plus cisplatin groups are consistent with a protective effect, likely related to antioxidant compounds in the extract. Previous work has also reported protective or biochemical effects of M. paradisiaca peel preparations in liver injury and oxidative-stress models.[16-18]

The absence of a significant difference between the 285 mg/kg and 570 mg/kg EEKBP plus cisplatin groups is important. The present data should be interpreted as evidence of protection compared with cisplatin alone, rather than as proof of a dose-response relationship. Additional work with a larger sample, a 570 mg/kg extract-only group, quantified oxidative-stress markers, and adjusted post hoc testing would be needed to define the optimal dose.

Histological findings

Qualitative histological appearances are shown in Figure 1. Group A showed predominantly normal hepatocytes, sinusoids, and central veins, without obvious interstitial bleeding or inflammatory-cell infiltration. Group B showed signs of liver injury, including hepatocyte nuclear lysis, incomplete cellular structure, vascular congestion, interstitial bleeding, and inflammatory-cell infiltration. Group C was broadly similar to the normal group, with only limited inflammatory-cell infiltration. Groups D and E showed qualitative improvement compared with Group B, with more dominant normal hepatocyte morphology and less severe bleeding, congestion, and inflammatory-cell infiltration.

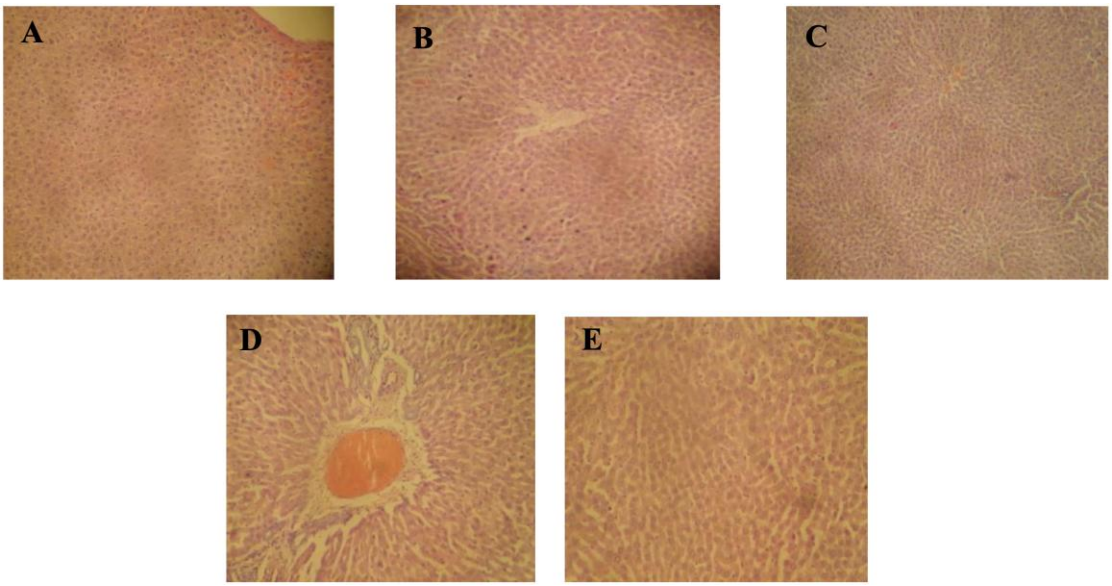

Figure 1. Histology images of liver tissue stained with hematoxylin and eosin at 400x magnification. Group A: normal; Group B: cisplatin only; Group C: EEKBP 285 mg/kg body weight; Group D: EEKBP 285 mg/kg body weight plus cisplatin; Group E: EEKBP 570 mg/kg body weight plus cisplatin.

The histological findings support the biochemical results. Cisplatin-induced liver injury has been associated with hepatocyte degeneration, necrotic areas, sinusoidal dilatation, inflammatory-cell infiltration, and oxidative-stress-related cellular damage.[4,5,12,19] The improvement observed in the EEKBP-treated groups may reflect antioxidant activity that helps maintain redox balance and reduce tissue damage. Nevertheless, the histological evaluation in this study was qualitative. Future studies

should add blinded scoring and biochemical markers such as malondialdehyde, superoxide dismutase, catalase, glutathione, and inflammatory markers.

CONCLUSION

Ethanol extract of Kepok banana peels contained flavonoids, saponins, tannins, and glycosides. In rats with cisplatin-induced hepatotoxicity, EEKBP was associated with lower SGPT and ALP levels and qualitative histological improvement compared with cisplatin alone. The findings support the hepatoprotective potential of EEKBP, but the two tested EEKBP plus cisplatin doses did not differ significantly from each other. Further studies with larger samples, quantitative histology, oxidative-stress markers, and formal dose-response analysis are needed before the extract can be advanced as a protective intervention.

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AUTHORS CONTRIBUTIONS

Maya Safriana Lubis prepared the samples, designed and executed the experimental protocol, analyzed the data, and drafted the manuscript. Ermi Girsang and Linda Chiuman supervised the study, reviewed the manuscript, and approved the final version. All authors read and approved the manuscript.

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DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

DISCLOSURE STATEMENT

The authors declare no conflict of interest.

AI-ASSISTED STATEMENT

A generative AI assistant was used for language editing. The authors reviewed and take responsibility for the final scientific content and references.

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