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Protective Effect of Banana, Cassava, and Corn Flours on Hepatotoxicity of Malnourished Male Rats

Efek Protektif Tepung Pisang, Singkong dan Jagung terhadap Hepatotoksisitas Tikus Jantan Malnutrisi

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ABSTRACT

Background: Malnutrition-induced hepatotoxicity is defined as liver damage caused by insufficient nutrition, which results in oxidative stress and damage to liver cells.
Objectives: The present study aimed to investigate the protective effects of banana, cassava, and corn flours on hepatotoxicity induced by malnutrition in male rats.
Methods: Twenty-four male rats were divided into six groups (n=4): (1) rats received 30 g/rat normal feed daily for 45 days; (2) rats received 30 g malnutrition feed daily for 45 days; rats received 30 g/rat malnutrition feed daily for 15 days and then treated with normal feed (3), banana flour (4), cassava flour (5), and corn flour (6), for 30 days. The malnutrition groups received a diet with protein deficiency for 15 days, then were treated with a diet according to each treatment group. The liver enzymes were analyzed, including aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. Furthermore, the liver's histopathological changes in each group were evaluated using Hematoxylin eosin staining.
Results: The AST levels in malnourished male rats significantly ($p<0.05$) increased (240.75±67.23 U/L) compared to the control group (170.00±33.52 U/L). While, the ALT levels (66.75±12.69 U/L) were decreased compared to the control group (98.75±26.61 U/L). Furthermore, malnutrition diet in rats caused significant changes in liver histology, including inflammatory cell infiltration, necrosis, congestion of the central vein, cytoplasmic vacuolization, and widened hepatic sinusoid. Interestingly, normalized AST and ALT levels and improved liver histology were observed in malnourished rats after receiving normal feed and flour of banana, cassava, and corn.
Conclusions: Banana, cassava, and corn flours exhibited hepatoprotective activity on malnutrition-induced hepatotoxicity in malnourhised male rats.

INTRODUCTION

Insufficient protein consumption or absorption causes protein malnutrition, which leads to pathophysiological alterations affecting many human tissues[1]. These changes may possess a long-term impact on tissue structure, function, and metabolism[2]. Furthermore, individuals experiencing protein malnutrition exhibit elevated levels of oxidative stress, potentially causing dysfunction within specific organelles[3]. Malnutrition is linked with metabolic stress, and due to the role of the liver as a significant metabolic organ, it will be associated with alterations in the hepatic metabolome, indicating oxidative stress[4]. Liver diseases can be triggered by various factors, including malnutrition, with initial stages marked by oxidative stress and inflammation. This process may eventually lead to the development of fibrosis, cirrhosis, and hepatocellular carcinoma[5].

Aspartate aminotransferase (AST) and *alanine aminotransferase* (ALT) are enzymes mainly found in liver and heart cells and also in the kidney, muscle, and pancreas in smaller quantities. When the liver or heart is damaged, these two enzymes are released into the bloodstream, resulting in high levels of these enzymes[6]. Malnutrition inhibits AST, ALT, and bilirubin production, impacting liver function. Furthermore, malnutrition can reduce endogenous enzymes in the body, disrupting the health and physiological condition of organs in malnourished individuals[7]. The prevention of liver cell damage is needed to provide antioxidant intake from outside sources, including plant compounds.

Effective antioxidant systems can regulate the balance of free radicals in the body[8]. Fruits and vegetables are high in phenolics, flavonoids, and carotenoids, which contribute significantly to antioxidant activities[9]. Bananas are one of the selected medicinal plants that boost antioxidant systems packed with

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beneficial compounds such as phenolics, carotenoids, biogenic amines, and phytosterols, which possess antioxidant properties that help shield the body from oxidative stress, contributing positively to human health[10]. Bananas are also known for their hepatoprotective properties due to their alkaloids, phenols, flavonoids, tannins, and saponin content. These compounds provide antioxidant, anti-diabetic, anti-cancer, anti-inflammatory, and anti-microbial benefits[11]. Phenolics and flavonoids improve the histological structure, suggest potential as hepato-protective agents, and significantly reduce biochemical and immunohistochemical parameters, returning them to near-normal levels[12,13].

Cassava is a native plant that potential to improve malnutrition and enhance access to a healthy and balanced diet by providing large amounts of protein and other essential nutrients[14,15]. Cassava is rich in anthocyanin and exhibits antioxidant, anti-inflammatory, and other biological activities[16]. Malnutrition can be improved using corn flour, a corn-soybean mixture that has been proven to be quite effective in treating cases of moderate acute malnutrition[17]. Corn contains fiber, essential amino acids, and micronutrients (vitamin A, zinc (Zn), and iron (Fe)) and can be used to combat malnutrition[18,19]. The high antioxidant capacity demonstrated by corn peptides suggests significant potential for them to serve as natural antioxidants in nutrition[20]. Previous studies found that the formulation of corn seeds, soybeans, and ripe bananas met the standards for therapeutic food use to treat acute malnutrition problems[21]. Therefore, the current study aimed to investigate the protective effects of banana, cassava, and corn flours on hepatotoxicity induced by malnutrition in male rats.

METHODS

Flour Preparation

Bananas (*Musa paradisiaca*), cassava (*Manihot esculenta*), and corn (*Zea mays* L.) were cleaned before being processed into flour separately. Plants are blanched with hot steam for 5 min. Then, plants were cooled, peeled, drained, and sliced using a manual slicer of approximately 0.5 cm in size. The plant slices were dried using an oven at 55°C for 6 h. The dried plant's slices were mashed using a grinder and sifted using an 80-mesh sieve[23]. The banana, corn, and cassava flour were administered as food to the experimental animals (30 g/rat/day). Careful monitoring was performed daily to ensure all animals consumed an adequate amount of the flour. Furthermore, any uneaten portions were measured and recorded to verify consumption levels.

Research Design and Animal Experimental

All experimental protocols in this research were approved by the Health Research Ethics Committee, State Polytechnic of Health Malang (approval number 802/KEPK-POLKESMA/2023). The research design of this research is shown in Figure 1. Adult male Wistar rats (100 ± 20 g), 7 weeks old, were obtained from the Malang Murine Farm and received a commercial diet for one week under controlled conditions with unrestricted access to diet and water ad libitum. The animals were randomly divided into six groups (n=4): (1) rats received 30 g normal feed daily for 45 days; (2) rats received 30 g malnutrition feed daily for 45 days; rats received malnutrition feed (30 g) daily for 15 days and then treated with normal feed (3), banana flour (4), cassava flour (5), and corn flour (6), for 30 days. The malnutrition diet consisted of tapioca flour 10 g/30 g + corn husk 20 g/30 g + corn oil 5 g/30 g + mixed vitamins and minerals 0.015 g/30 g. The banana flour microbial-directed complementary food (MDCF) consisted of banana flour 9.37 g/30 g + tempeh flour 3.75 g/30 g + chickpea flour 3.75 g/30 g + peanut flour 3.75 g/30 g + corn oil 3.75 g/30 g + sucrose 5.62 g/30 g + micronutrient mix 0.015 g/30 g[22]. It is like other processing groups, but banana flour is replaced with cassava and corn flour. After treatment, the animals were anesthetized with ketamine (Pfizer, purchase from PT Ekapharindo Putramas) and dissected quickly.

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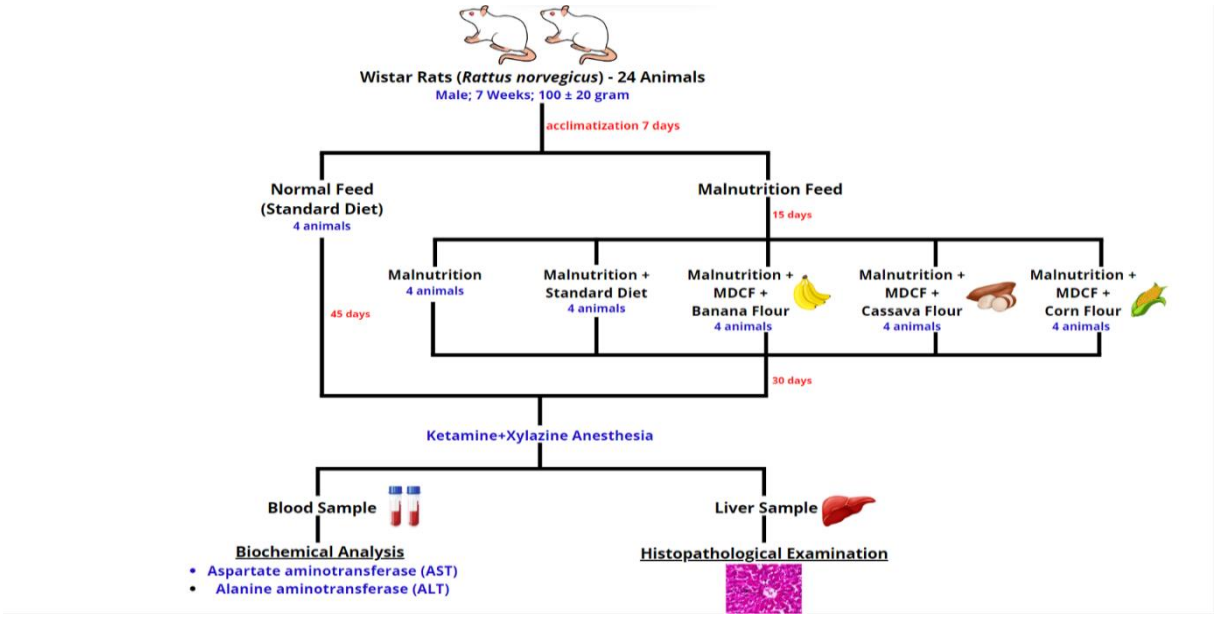

Figure 1. Research Design

Indicators of Malnutrition

Body weight and hair growth were used as indicators of malnutrition. Body weight and morphological parameters were observed every week. Malnourished experimental rats with weight loss and unhealthy hair growth were compared to healthy animals.

Hepatotoxicity Evaluation

Collection of Blood Serum

Blood was directly isolated from the rat's heart. The blood sample was placed in a tube without an anticoagulant at room temperature (37°C) for one hours. The clotted blood was centrifuged at 3000 rpm, 4°C for 15 min. The serum was collected and stored in a deep freezer at -24°C for further analysis.

Biochemical Analysis

The liver enzymes, including *alanine aminotransferase* (ALT), and *aspartate aminotransferase* (AST) were assessed using DIALAB GOT (AST), Mod. IFCC, DIALAB GMBH with an IFCC (International Federation of Clinical Chemistry) kinetic examination method at 340 nm. The concentration of ALT and AST was done in the Pathology Laboratory, Faculty of Medicine, Brawijaya University, Malang. This assessment measured the levels of ALT and AST in the blood serum to evaluate the biochemical activities associated with liver function.

Histopathological Examination

The livers of rats were isolated and weighed. Then, the liver was cut into small pieces and fixed with 10% formalin for 24 h. Liver was cleaned with running water and preserved in 70% ethyl alcohol. Samples were dehydrated, cleared, and embedded in paraffin wax. Paraffin blocks were cut with 5 microns thickness using a rotary microtome and stained with hematoxylin and eosin. Liver sections were observed using an Olympus microscope type CX33 (Olympus, Japan) and Olympus SZ61 EP50 camera (Olympus, Japan).

Statistical Analysis

Data were analyzed statistically using one-way analysis of variance (ANOVA). The biochemical data were reported as mean ± S.D. Statistical analysis was conducted using SPSS 22.0 for Windows software with a p-value of <0.05.

RESULTS AND DISCUSSIONS

Body Weight Changes

Figure 2A showed that malnutrition led to a significant decrease in body weight of male rats compared to the control group (-21.51±3.20 versus 61.63±53.94%). During the treatment period, the decrease in body weight of malnourished rats continued until the end of treatment (Figure 2B). Interestingly, the body weight variation was significantly increased in malnourished rats fed with normal feed. Body weight gain was also improved in malnourished rats fed with banana, cassava, and corn flour (Figure 2B). The negative value in body weight variation suggests weight loss (Table 1).

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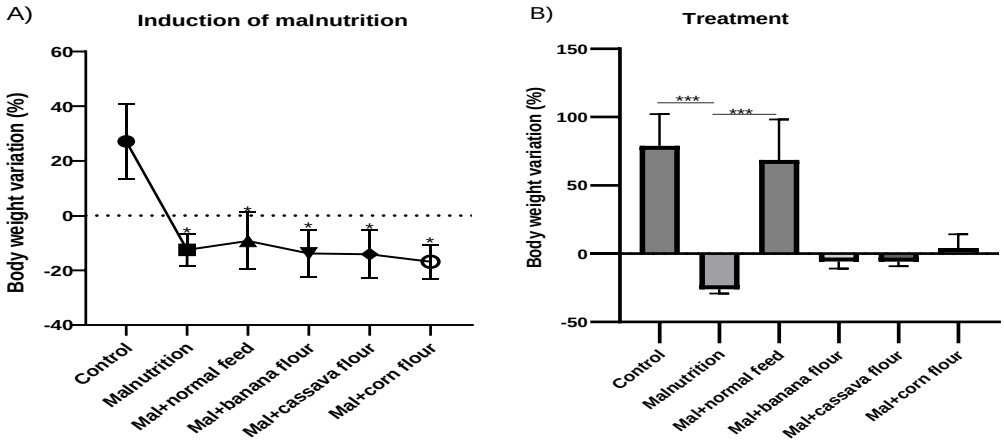

Figure 2. The changes in body weight variation **(A**) During the malnutrition and **(B**) During the Treatment Period.

Table 1. The Changes in Body Weight Variations in All Treatment Groups.

Groups	Body Weight Variation (%)
Control	61.63±53.94
Malnutrition	-21.51±3.20[a]**
Malnutrition with normal feed	42.62±38.00[b]*
Malnutrition with banana flour	-2.60±4.54
Malnutrition with cassava flour	-3.00±11.63
Malnutrition with corn flour	-1.70±5.62

Values are mean ± standard deviation (SD) from four rats in each group). (*) Statistically Significant (P<0.05). a: significantly different from the control group, b: significantly different from the malnutrition group

Evaluation of Liver Enzymes

The liver function was also affected after malnutrition diet induction, as indicated by changes in serum levels of AST and ALT compared to control animals. Malnutrition diet administration (30 g/day) for 15 days significantly ($p<0.05$) caused a significant increase in AST levels in male rats compared to the control group (Table 2). Interestingly, the AST level in malnourished rats was significantly decreased ($p<0.05$) after 30 days of treatment with normal feed and flour of banana, cassava, and corn (Table 2). Furthermore, the ALT levels of male rats decreased after being fed a malnutrition diet and then improved after receiving normal and three kinds of flour. The decrease in AST and improvement in ALT levels at the same level as the control group are significant indicators of improved liver function in malnourished rats fed a diet containing normal feed and flour of banana, cassava, and corn.

Table 2. The Alteration of AST and ALT Enzyme Concentrations in All Treatment Groups.

Groups	ALT (U/L)	AST (U/L)
Control	98.75±26.61	170.00±33.52
Malnutrition	66.75±12.69	240.75±67.23[a]*
Malnutrition with normal feed	88.75±24.55	145.75±34.72[b]*
Malnutrition with banana flour	93.25±40.03	153.50±22.25[b]*
Malnutrition with cassava flour	87.00±34.59	180.00±35.79[b]*
Malnutrition with corn flour	79.50±23.01	175.25±28.45[b]*

Values are mean ± standard deviation (SD) from four rats in each group). (*) Statistically Significant (P<0.05). a: significantly different from the control group, b: significantly different from the malnutrition group, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase.

Liver Histology Results

The livers of the control group showed normal hepatic lobules with a uniform pattern of polyhedral hepatocytes, forming cords of hepatocytes that extend in the direction from the periphery of the liver lobule to the central vein. In this arrangement, at least one cell surface borders a sinusoid vessel (Figure 3a). The liver sections of the rats treated with malnutrition fed for 15 days showed disrupted histological architecture with cytoplasmic vacuolization, widened sinusoid, congestion in the central vein, venous dilatation, infiltration of inflammatory cells around the central vein, hemorrhage, and necrosis of other liver cells compared to the control group (Figure 3b). The groups treated with malnutrition for 15 days followed by regular feed, flour of banana, cassava, and corn administration showed a significant improvement in the histological, indicated by normal cells with little cytoplasmic vacuolization, slight congestion in the central vein, and slight necrosis (Figure 3 c, d, e, and f, respectively).

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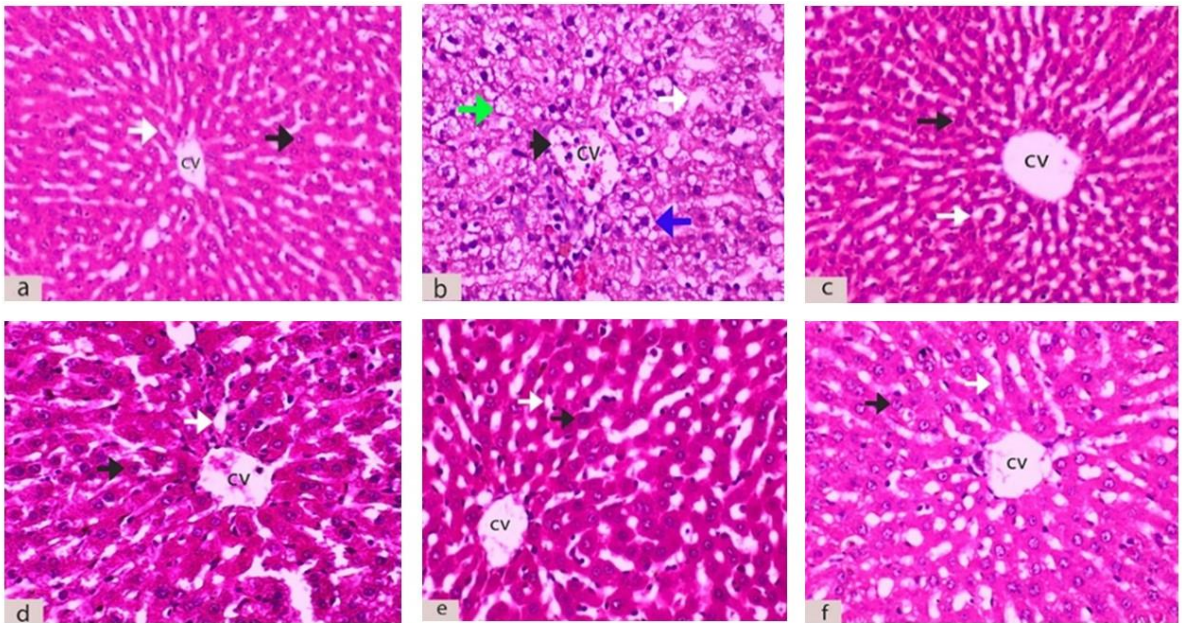

Figure 3. The examination of histological changes in the liver of all treatment groups. (a) The control group shows a uniform pattern of polyhedral hepatocytes radiating from the central vein with normal sinusoid space. (b) The malnutrition group shows damage and congestion of the central vein, and many hepatocytes are in alteration and degeneration states. Inflammatory cell infiltration around the central vein (arrowhead), hepatocytes with cytoplasmic vacuolization (blue arrow), necrosis in hepatocytes (green arrow), and widened hepatic sinusoid. (c, d, e, f) The malnourished rats + normal feed, banana, cassava, and corn flour, respectively, show better improvement in liver architecture with little vacuolization and necrosis and no congestion in the central vein. Hepatocytes (black arrow); sinusoid (white arrow); central vein (CV). (H&E, magnification 400X).

The current study focused exclusively on reducing protein intake while maintaining sufficient quantities of other macronutrients and micronutrients. The control group received an adequate protein diet, and the malnutrition group received a protein-deficient diet. All experimental groups received same food quantities and adhered to recommended daily minimums for micronutrient consumption. Malnutrition has been used to induce liver injury in experimental animal models. Therefore, the alteration in experimental animals predominantly originated from the reduction in protein intake.

The hepatotoxicity and liver damage caused by malnutrition in the liver of rats were evaluated by examining several parameters, including changes in body weight, liver function markers, and histological changes in the liver. The rats subjected to a protein-deficient diet displayed a significant reduction of approximately 21% in their initial body weight after 45 days, indicating malnutrition. Similar findings were reported by de Oliveira et al. (2014), which found reduced body weight and serum albumin levels in mice on low-protein diets compared to control groups[24]. Jansson et al. (2006) suggested that the catabolic state and the breakdown of fat and protein stores cause low weight gain[25]. The liver plays a pivotal role in various metabolic processes, and prolonged periods of malnutrition impose heightened stress upon hepatic functions, leading to significant body weight loss, likely due to reduced glycogen and protein levels in the liver and muscles[26]. The current study showed an inverse correlation between AST enzyme level and body weight in malnutrition rats, suggesting an impact of the nutritional status on the liver tissue. Harris et al. (2013) also reported a link between malnutrition and elevated AST levels linked to weight loss in anorexic individuals[27]. Restoring weight through refeeding was associated with a decline in this enzyme level. This confirms the direct impact of nutritional status on hepatic enzymes and body weight, as explained in our study. These results reflect those of Wojciak (2014), who also found the effect of malnutrition on liver indicators, decreased body weight, and increased physical activity in malnutrition rats[28].

The liver represents the largest gland in the body, controlling many biological processes that require energy, such as biosynthesis, excretion, detoxification, and metabolism of various compounds. In cases of massive cellular loss, the liver can regenerate through cell proliferation, but this process may fail if the loss exceeds certain limits, resulting in liver damage. Oxidative stress can be exacerbated by malnutrition and cause tissue injury in several organs, especially the liver. Therefore, these malnutrition-induced changes are reflected in chemical parameters and histological changes. This study showed that the group of rats subjected to malnutrition suffered liver damage, observed through an increase in AST level and a decrease in ALT level, which are essential to biological processes compared to the control group. Furthermore, our observations were supported by severe histological changes in the liver tissue, providing evidence of malnutrition-induced hepatic injury. This is consistent with previous studies that found that malnutrition animals had a lower ALT level and a higher AST level compared to the control group[29]. In contrast, previous

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studies indicated a significant increase in ALP, ALT, AST, total proteins, and total bilirubin in malnutrition male Wistar albino rats[7].

Serum ALT is a liver-produced enzyme released into the bloodstream related to liver size and nutritional status. ALT increase is not a universal finding in protein-energy malnutrition in animal[30]. The lower levels of ALT found in malnutrition animals can be associated with factors such as frailty, sarcopenia, and decrease in liver functions, as well as age, severity of malnutrition, and a lower body mass index[31]. Notably, the activity of AST tends to increase or remain stable with age, while ALT activity decreases in elderly populations[32]. Lower ALT levels have also been associated with reduced albumin levels and higher mortality rates in heart failure patients, as identified by Ambrosy et al., (2015)[33]. The association between lower BMI or body fat with reduced ALT activity may indicate liver damage in the case of malnutrition, as AST tends to increase more than ALT because AST is predominantly found in the centrilobular region[34]. Moreover, malnutrition can be linked to pyridoxine deficiency, which can lead to decreased ALT levels. The reason is due to hepatic deficiency of pyridoxal 5'-phosphate, a cofactor of the enzymatic activity of ALT[35]. This further underscore the clinical significance of ALT as a potential marker for identifying and assessing malnutrition in various medical contexts.

An imbalance in the levels of these enzymes is a marker of liver cell dysfunctions and damage. These enzymes are located within the hepatocyte cytoplasm, and any damage to these cells results in the release of these enzymes into the bloodstream, leading to elevated levels[36]. Malnutrition can alter the plasma membrane of the hepatocyte and a lose its functional integrity, increasing the permeability of plasma membranes, which explains the observed rise in AST enzyme levels in the blood of rats[37]. Leakage of these enzymatic substances into the bloodstream when liver dysfunction indicates the extent of liver damage[38]. The results of the current study are consistent with a previous study indicating a relationship between malnutrition and liver enzymes[39], and the relationship between malnutrition and conditions such as hepatitis, oxidative stress, and liver dysfunction[40,41]. This evidence underscores the profound impact of malnutrition on liver health and highlights the importance of monitoring liver enzymes as valuable indicators of hepatotoxicity in protein malnutrition.

Malnutrition can lead to oxidative stress, a condition where there is an imbalance between the production of harmful free radicals and the body's ability to neutralize them with antioxidants due to a disorder of antioxidant enzymes, damaging liver cells and impairing their functionality. This has been noticed in malnutrition-induced hepatitis in rats exposed to food restriction[42]. A study found that starvation can cause oxidative stress to increase by weakening antioxidant defense mechanisms[43,39]. Reduced nutrient intake can lead to alterations in the hepatic metabolome, indicating oxidative stress, overproduction of ROS, and deficiency of hepatic antioxidants[4]. Elevated ROS concentrations and free radicals can significantly damage cell structures, nucleic acids, lipids, and proteins[44], culminating in cellular injury and necrosis within the liver. Necrototic cells empty their contents into the bloodstream, resulting in increased transaminase activity, exemplified by the increased levels of AST. Previous studies had shown an increase in AST and ALT levels in the serum of the mice when oxidative stress injury, then the levels of the enzyme improved after treatment with antioxidants[45].

One of the mechanisms underlying malnutrition-induced liver damage is a decrease in insulin secretion, which raises blood glucose levels and, thus, a disruption of antioxidant enzymes. This is confirmed by previous research that found a significantly lower plasma insulin level in malnutrition young adult patients[46], and in malnutrition male Wistar rats[47], as well as, increased glucagon release, leading to the release of glucose into the bloodstream, breakdown of hepatic glycogen, and an increase in autophagic vacuoles in the liver tissue[26,27]. Moreover, Oboh et al. (2015) found that hyperglycemia can cause oxidative stress due to ROS production, further affecting liver and pancreas function in malnutrition individuals[48]. Research on malnutrition and diabetic rats has shown a link between low antioxidant enzyme activity and reduced insulin, where they experienced disturbances in antioxidant enzyme activity. Importantly, refeeding and insulin injections showed the potential to improve enzyme disorders[49,43,50]. Malnutrition has an immunological aspect, individuals with malnutrition and Type 2 diabetes mellitus tend to have significantly higher levels of adiponectin and adipsin and significantly lower levels of leptin, Type 1, Type 2, Type 17, pro-inflammatory and regulatory cytokines[51]. These changes in cytokine levels are important because they indicate potential immunomodulatory effects on the liver, which can further influence liver function and susceptibility to damage.

The results of this study suggest that there is a need to overcome liver damage resulting from malnutrition. This would help avoid possible complications in the liver's metabolic activities involving the enzymes AST and ALT. Various plants rich in bioactive substances are used in foods for health benefits. Many studies have been carried out to determine the effect of antioxidants on improving liver disease. Natural antioxidants play a key role in reducing oxidative stress by scavenging excess free radicals[52]. Antioxidants have emerged as a therapeutic option for treating and preventing lifestyle-related diseases. The research focuses on assessing the potential of banana, cassava, and corn flours as protective agents against liver diseases and their potential to mitigate the harmful effects of malnutrition on liver function in malnutrition animal models. The study found that rats treated with banana, cassava, and corn flour showed improvements in body weight, lower AST levels, and higher ALT levels up to the level of the control group compared to malnutrition animals, which may be because liver cells heal and regenerate. Additionally, the liver histopathology results confirmed these plants' protective activity, as evidenced by the mild reversal of malnutrition-induced necrosis, inflammation, and congestion. Our results provide the first experimental evidence that flour from bananas, cassava, and corn improves hepatic cell damage induced by malnutrition in male rats.

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Malnutrition-induced liver damage resulted in raised AST levels, which are indicative of cellular leakage. Treatment with these plants resulted in the recovery of raised AST levels due to the stabilization of the plasma membrane of the hepatocytes, which re-established its structural integrity. This may be due to several protective antioxidant compounds, which enhance the liver's regeneration ability. Vitamin C is an antioxidant that works in the cytosol outside the cell and is essential for preserving the integrity of cell membranes[53]. Additionally, liver tissue could improve by reducing necrosis and fatty accumulations, removing congestion, reducing oxidative stress, and strengthening the immune system.

Agung banana is a source of energy as it contains a high percentage of protein, carbohydrates, and fats[23]. The banana plant is considered one plant that contains many bioactive compounds, including a high number of phenolic compounds such as catechin, epicatechin, lignin, anthocyanin, and tannin. All these bioactive compounds possess antioxidant properties[54,55]. Bananas contain polyphenols and flavonoids that exhibit strong antioxidant properties, exert a strong radical scavenging activity[56]. Flavonoids such as quercetin have demonstrated significant improvements in attenuating oxidative damage by inhibiting mitochondrial malfunction and oxidative stress, as well as the scavenging of oxygen radicals, leading to cytoprotective effects[57,58]. It also can enhance APOA1 and HMOX1, lipid peroxidase inhibitors, and provide cardioprotective and hepatoprotective effects[59]. Rutin is a flavonoid compound found in bananas, which has antioxidant, cytoprotective, and neuroprotective capacities[57]. Moreover, Quitete et al. (2021) reported that regular consumption of phenolic-rich bananas can improve liver antioxidant status and prevent metabolic disorders[60]. Banana flour has also been found to protect the liver from damage caused by malnutrition because it contains hepatoprotective phenolic compounds, and incorporating it into a high-calorie diet Improves liver damage markers AST and ALT[61]. These results are in line with Shian et al. (2012) who reported that the banana fruits have antioxidant properties[62]. These findings highlight the therapeutic potential of banana flour in reducing liver damage induced by oxidative stress and inflammation in malnourished animals.

Banana flour may enhance antioxidant enzymes and improve liver function. According to Abdul Gofur et al. (2019), antioxidant could improve insulin sensitivity by lowering necrosis, increasing SOD, and enhancing insulin and IRS-1 expression, thus improving the activity of antioxidant enzymes[63]. Additionally, banana extract exhibits positive effects in diabetic rats where it acts as an antidiabetic by restoring hepatic enzymes AST, ALT, ALP, and hexokinase to normal levels and preventing oxidative damage through increased antioxidant activity[64]. Moreover, the consumption of green banana flour has been associated with a reduction in glucose level[65]. Therefore, bananas can be used as potential treatments for hepatotoxicity and liver damage caused by malnutrition by reducing insulin resistance and enhancing antioxidant defenses.

The present study revealed that malnourished rats treated with cassava and corn flour exhibited significant changes in AST and ALT levels as well as liver histological structure. This is in line with previous research indicating that the addition of whole grains from sorghum and durum wheat to cassava flour enhances antioxidant properties, protein, and fiber content[66]. This could be caused by cassava's antioxidants, proteins, and fiber content. It can inhibit pro-inflammatory cytokines while also repairing the damage caused by malnutrition. Cassava contains anthocyanins that have antioxidant, anti-inflammatory, anti-cancer, and other biological properties[16]. Gofur et al. (2018) found that anthocyanin has antioxidant properties since it inhibits ROS production[67]. Anthocyanin supplementation improves liver function in mice by enhancing antioxidants and increasing β-oxidation. This reduces mitochondrial dysfunction and thus inhibits the activation of inflammatory pathways and reduces oxidative stress[68]. Cassava is also rich in secondary metabolites with antioxidant properties, and its leaves can be used as anti-inflammatory and anti-cancer agents due to their high amygdalin content, as indicated by Didagb et al. (2023)[69]. Moreover, Kareem et al. (2022) found that cassava contains carotenoids, phenols, and flavonoids with antioxidant and anti-hyperglycemic properties[70]. Flavonoids are potent antioxidants that effectively prevent free radical oxidation. The quantity and arrangement of hydroxyl groups influence an antioxidant's capacity[71]. Rutin content is high in the cassava plant[72]. The chemical structure of rutin is characterized by polyphenol hydroxyl groups that bind to free radicals[73]. Furthermore, rutin has been found to protect liver cells from free radical damage, allowing damaged enzymes to continue functioning and maintaining the cell membrane's integrity[74]. Cassava leaves exhibit antioxidant properties, scavenging free radicals and inhibiting pro-inflammatory cytokines such as IL6, TNF-α, Monocyte MCP-1, PGE2, and nitric oxide[75]. Elshamy et al. (2021) found that the use of cassava shoot water extract can reduce liver enzymes and increase antioxidant levels[76].

The study revealed that corn flour could improve liver functions by altering the levels of AST and ALT to normal conditions. Lv et al. (2013) found that corn peptides could increase rat liver through decreased ALT and AST levels, significantly reduced transforming growth factor-β1, nitric oxide, malondialdehyde levels, and hydroxyproline, as well as reduced inflammation and fibrosis. Moreover, serum albumin levels and total antioxidant capacity can be increased by increasing the activity of the superoxide dismutase enzyme in the liver[77]. Selenium-biofortified corn peptides work against liver injury because corn has high antioxidant activity. It works by reducing hydrogen peroxide, which prevents the release of immune factors such as IFN-γ and TNF-α[78]. A previous study discovered that corn peptides, considered bioactive, can protect the liver and significantly mitigate fatty liver injury. This is manifested through reducing blood lipid and hepatic cell levels, mitigating insulin resistance, and preventing oxidative stress by reducing ROS production[79]. Therefore, corn peptides are a potential alternative treatment for

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malnutrition-induced liver fibrosis. These properties collectively contribute to preventing liver disorders and supporting antioxidant functions by suppressing oxidative stress. Our findings demonstrated that using plants with antioxidant and anti-inflammatory properties, such as cassava and corn, improves liver function, including AST and ALT levels.

CONCLUSIONS

The results indicated that malnutrition could increase AST levels, decrease ALT levels, and lead to histopathological changes in the liver tissue of male rats. Bananas, cassava, and corn flours have protective effects on the liver of malnourished male rats by improving the enzyme levels of ALT and AST to normal and altering histological changes in the liver. So, the research about malnutrition must be continued more and find a solution to mitigate its damage and conduct more studies on these plants in terms of their therapeutic effects.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

All authors have no conflict of interest in this article.

AUTHOR CONTRIBUTIONS

Conception and design: SRL, YR Analysis and interpretation of the data: NM, SRL, HS, YR. Drafting of the article: NM, SRL, HS, YR. Critical revision of the article for important intellectual content: NM, SRL, HS. Final approval of the article: NM, SRL, HS, YR. Provision of study materials: SRL. Obtaining of funding: SRL Administrative, technical, or logistic support: SRL. Collection and assembly of data: NM, SRL, HS, YR.

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