



THE EFFECT OF BANANA-BASED ANALOG RICE ON KIDNEY HISTOPATHOLOGY IN RATS FED A HIGH FAT AND FRUCTOSE DIET

Efek Beras Analog Berbasis Pisang terhadap Histopatologi Ginjal Tikus dengan Diet Tinggi Lemak dan Fruktosa

Nahiza Atmaningtyas¹, Sugiyanta², Ayu Munawaroh Aziz³, Hairrudin²

¹Pendidikan Dokter, Fakultas Kedokteran, Universitas Jember, Jember, Jawa Timur, 68121

²Lab Biokimia, Fakultas Kedokteran, Universitas Jember, Jember, Jawa Timur, Indonesia 68121

³Lab Histologi, Fakultas Kedokteran, Universitas Jember, Jember, Jawa Timur, Indonesia 68121

E-mail: sugiyanta97.fk@unej.ac.id

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ABSTRACT

High Fat and Fructose Diet (HFFD) can cause hypercholesterolemia and kidney damage, which may be reduced by banana-based rice analogs due to low glycemic index, high fiber, pectin, and phenolic. The aim of this study is to assess the effect of banana-based analogue rice on kidney histopathological features in HFFD-fed rats (*Rattus norvegicus*). This study is a true experimental post-test only design on 24 male rats randomly divided into negative control (CN) and HFFD groups for 14 days. HFFD-fed rats group then received standart pellets (CP), white rice pellets (WR), and banana-based analog rice pelletes (BAR) for 21 days. Kidneys were examined microscopically (400x) for inflammatory cell infiltration, edema, and necrosis in the glomerulus and renal tubules. This study showed the average kidney damage scores from highest were: WR group (5.4), CP group (5.3), BAR group (3.2), and CN group (2.5). Then One-Way ANOVA and Post-Hoc Bonferroni test showed a significant difference between BAR group with CP and WR groups. Banana-based analog rice pellet improved kidney condition in rats, which kidney damage scores in the BAR group being 60 percent lower than CP and WR groups. Future studies should consider serial termination and necropsy to evaluate kidney damage progression.

Keywords: banana analog rice, dyslipidemia, HFFD, kidney histopathology

ABSTRAK

Diet tinggi lemak dan fruktosa (HFFD) dapat menyebabkan hiperkolesterolemia hingga kerusakan ginjal, yang dapat dihambat dengan beras analog berbasis pisang karena memiliki indeks glikemik rendah, tinggi serat, pektin dan fenolik. Penelitian ini bertujuan menilai efek beras analog berbasis pisang terhadap gambaran histopatologi ginjal pada tikus (*Rattus norvegicus*) dengan HFFD. Penelitian ini berdesain *true experimental* dengan *post-test only* pada 24 tikus jantan (*Rattus norvegicus*), yang secara acak dikelompokkan dalam kelompok kontrol negatif (CN) dan perlakuan HFFD selama 14 hari. Kelompok dengan HFFD selanjutnya dibagi dan menerima pelet standar (CP), pelet beras putih (WR), dan pelet beras analog berbasis pisang (BAR) selama 21 hari. Kemudian ginjal diamati menggunakan mikroskop (400x) untuk menilai infiltrasi sel inflamasi, edema, dan nekrosis pada glomerulus serta tubulus ginjal. Penelitian ini menunjukkan rerata kerusakan ginjal dari yang terberat adalah kelompok WR (5,4); kelompok CP (5,3), kelompok BAR (3,2); kelompok CN (2,5). Uji *One-Way ANOVA* dan *Post-Hoc Bonferroni* menunjukkan perbedaan signifikan antara kelompok BAR dengan kelompok CP dan WR. Pemberian pelet beras analog berbasis pisang memberikan perbaikan pada ginjal tikus dengan nilai kerusakan ginjal kelompok BAR lebih rendah 60 persen dibandingkan dengan kelompok CP dan WR. Penelitian selanjutnya disarankan melakukan terminasi dan nekropsi secara serial guna mengevaluasi progresivitas kerusakan ginjal.

Kata kunci: beras analog pisang, dislipidemia, HFFD, histopatologi ginjal

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INTRODUCTION

High Fat and Fructose Diet (HFFD) is a diet that generally consists of more than 50 percent of calories from fat and fructose.¹ One kind of food that consist high fat is eggs, especially quail eggs which have a fat content of 10-15 percent of their total weight and in 100 grams of quail egg yolk contains 31.8-35.5 grams of fat.² The recommended intake if chicken eggs in healthy individuals is 1-3 eggs with a average weight of 60 grams per egg with calories of 72 kcal which contain cholesterol levels of 423 mg/dL.^{3,4,5} Meanwhile, quail eggs weigh an average of 9 grams per gain with calories of 14 kcal and 844 mg/dL cholesterol, which is higher than chicken eggs but lower number of calories.³ High fructose content is also found as a sweetener in sweet drink such as carbonated drinks which contain 34 grams of sugar in every 330 ml and produce 140 kcal.^{6,7}

Minister of Health regulation No. 30 of 2023 states that the daily intake limit for fat is less than 67 grams or five tablespoons of oil and sugar is less than 50 grams or four tablespoon in each individual.⁸ A diet with high fat and fructose levels causes an increase in total cholesterol, low-density lipoprotein (LDL), triglycerides (TG), and a decrease in high-density lipoprotein (HDL) levels in blood plasma which is a sign of lipid metabolism disorder that trigger dyslipidemia.^{6,9,10}

The World Health Organization estimated that in 2008, the prevalence of dyslipidemia in sequence from the highest in the world was in Europe (53.7%), America (47.7%), Southeast Asia (30.3%), and Africa (23.1%).¹¹ Meanwhile, in Indonesia itself, based on RISKESDAS data, Indonesia has a prevalence of dyslipidemia of 28.8 percent in the population aged ≥ 15 years with cholesterol levels > 200 mg/dL.¹²

Individual with high cholesterol diet and lower calories have been shown to have higher risk of death than individual with nutritionally balanced diets but higher calories, this proves that it is not only calories that count in a diet but also the balance of nutrients in food.¹³ But calories are needed by the body for daily metabolic, physical, and mental activities based on the average nutritional adequacy rate for Indonesians, the calories needed per day are 2100 kcal and if excess will be stored in the form

of fat which can trigger obesity.^{14,15} Obesity is closely related to dyslipidemia because it is risk factor that triggers the condition or worsens due to an individual's unbalanced diet.¹⁶

Dyslipidemia can lead to other adverse conditions such as diabetes mellitus (DM) which can results in complication retinopathy, neuropathy, nephropathy, and cardiovascular system disorder.^{17,18} Dyslipidemia has also been shown to be a risk factor for elevated liver enzymes which are an indicator of liver disfunction and also one of the triggers of chronic kidney disease (CKD).^{19,20} CKD occurs by a mechanism involving damage to kidney cells leading to decrease in glomerular filtration rate (GFR) caused by factors such as ischemia, toxicity, and oxidative stress.^{21,22,20}

Chronic kidney disease (CKD) can reduce an individual's quality of life through complications such as anaemia due to decreased erythropoietin synthesis, mineral disorders and bone abnormalities that can increase the incidence of fractures, and cardiovascular disease that can lead to sudden death.^{23,24,25} The worsening of conditions due to dyslipidemia can be inhibited by lifestyle modifications including a diet low saturated fat, high unsaturated fat, high in fibre, an low glycemic index to reduce total cholesterol, LDL, TG, and increase HDL.^{26,27,28}

Analogue rice is generally produced from a mixture of non-rice flour with higher nutritional profile and fibre content than white rice.²⁹ Research related to analogue rice made from modified cassava flour (MOCAP) has been shown to provide improvements in kidneys with hyperglycemia conditions due to its high fibre content and low GI.³⁰ One of the local resources similar to MOCAP with low glycemic index and high fibre content is banana. Immature bananas generally have a glycemic index value of 30 which is lower than ripe banana.³¹

Bananas give a hypocholesterolemic effect from the high fibre content and pectin which can help bind and reduce cholesterol absorption in the digestive tract.^{32,33} Every 100 grams of banana contain 2-18 grams of fibre and the recommended dietary fibre intake is 19-38 grams per day, so consuming 2 bananas will fulfil the daily fibre intake.³⁴ Banana have a high potassium and phenolic which can maintain blood pressure stability and prevent kidney

damage by reduce the level of reactive oxygen species (ROS).^{35,36}

Studies related to the effects of banana-based analogue rice on dyslipidemia are currently limited, so further research is needed, especially its effects on the histopathological features of the kidney. This study uses an animal model of male Wistar rats fed with HFFD. Rats that are induced orally with HFFD solution are found to have increased fat accumulation, increased cholesterol and TG levels that lead to dyslipidemia.³⁷

The objective of this study was to assess the effect of banana-based analogue rice on the histopathological features of kidney of rats (*Rattus norvegicus*) induced by high fat and fructose diet.

METHOD

Research Design

The study used was true experimental with Wistar rats (*Rattus norvegicus*). The research design used was simple random to divide the sample into negative control group (CN) and High Fat and Fructose Diet (HFFD) treatment group. CN group was fed with standart pellet and aquades at. libitum. Rats that were fed with HFFD and become dyslipidemia then devided by stratified random group into three groups, which were positive control group (CP), white rice group (WR), and banana-based analogue rice group (BAR). Each group were fed with standart pellet, white rice pellet, and banana-based analogue rice pellet.

Sample and Population

The data used in this study are primary data. The samples in this study were Wistar strain rats (*Rattus norvegicus*). Samples were selected based on inclusion criteria to obtain a homogeneous sample, those are: male, age 2-3 months, 150-250 grams, and physically healthy. Exclusion criteria in the study samples were rats that sick and died during the study. The number of samples was determined using Degree of Freedom formula with 10 percent of correction factor and obtained 6 rats for each group.³⁸ The total sample used was 24 rats divided into 4 groups.

Preparation of Dyslipidemia Rats

This study was held in June-December 2024 at the Laboratory of Pharmacology, Faculty of Medicine, University of Jember, while the observation of kidney histopathology was conducted at the Laboratory of Histology and Anatomical Pathology, Faculty of Medicine, University of Jember. This study has been approved ethically by the ethics committee of the Faculty of Medicine, University of Jember with No: 5326/UN25.1.10.2/KE/2024.

The rats selected to be the sample were adapted for 7 days before treatment and given standard pellet and drink ad libitum. After the adaptation period, the rats were divided by simple random into a negative control group (CN) of 6 rats and the rest into treatment groups that were induced with HFFD as much as 4 mL/200 grams of rat body weight by oral sonde once a day for 14 days. Each 4 mL of HFFD contains 1 mL of quail egg yolk, 1 mL of 60 percent fructose, and 2 mL of cooking oil. Both negative control group (CN) and treatment group will be given standard pellet feed and drink ad libitum in their maintenance. Mice with body weight >8 percent above normal body weight or 150-250 grams, at the end of HFFD treatment will be selected for further treatment.^{39,40}

Treatment of White Rice and Banana-Based Analogue Rice

All HFFD induced rats (n=18) with body weight >8 percent above normal body weight were then divided into 3 groups in proportionally stratified randomised manner.⁴⁰ Stratification was done based on body weight. The three groups were: positive control rats fed standard pellets (CP), dyslipidemic rats fed white rice pellets (WR), and dyslipidemic rats fed banana-based analogue rice pellets (BAR). Each rat was fed according to its group for 21 days ad libitum.

Pellets were produced at the Food Engineering Laboratory, Faculty of Agricultural Technology, University of Jember. White rice pellets were made by mixing white rice (IR64) and standard feed in a ratio of 3:2 which was then formed into pellets and given to the WR group. Banana-based analogue rice in this study is artificial rice with the main ingredients of banana, corn, and white rice (IR64) in a ratio of 3:3:4 which is processed by extrusion process.⁴¹

Table 1
Histopathological Scoring of Kidney Damage

Variabel	Skor
Glomerulus	
Normal	0
Found of inflammatory cell inflamation	1
Found of bowman space edema	2
Found of necrosis cell	3
Tubules	
Normal	0
Found of inflammatory cell inflamation	1
Found of epithelial tubules edema	2
Found of necrosis cell	3

Kidney Organ Collection, Preparation, and Observation

After 21 days of treatment, rats were sacrificed and anaesthetised using ketamine 75 mg/kg body weight and xylazine 5 mg/kg body weight, injected intramuscularly. Then the rats were dissected through the thorax with a Y type pattern, the kidney organs were taken. Kidney organs were processed into histopathological preparations using Haematoxylin Eosin (HE) painting and assessed for the level of damage based on scoring consisting of inflammatory cell infiltration, bowman space edema, tubular epithelial edema, and necrosis cells in the glomerulus and renal tubules with score range of 0-3 as in Table 1.⁴² Assessment was performed using an OptiLab light microscope with 400x magnification for 5 fields of view. The reading of kidney histopathology was performed in a double blinding manner with two observers

Data Analysis

The data were analysed using the SPSS application. Data were collected in the form of renal histopathological scoring values. Statistical tests of renal histopathological scoring using the One-Way ANOVA test to determine the significance ($p < 0.05$) of differences in histopathological images. Furthermore, to distinguish which groups have significant differences, a comparison of each group with other groups is carried out with the Bonferroni Post-Hoc test which will show significant results if it has a $p < 0.05$.

RESULT

The results of HFFD treatment of rats are proven to have an effect on the condition of rats based on weight gain. The average weight gain in each group obtained by the negative control group (CN) was the lowest while the group with white rice treatment (WR) was the highest. This is in accordance with the results of histopathological observations of the kidneys that show the lowest damage score is the negative control group (CN) while the highest damage score is the group with white rice treatment (WR).

Result of High Fat and Fructose Diet on Rats

After the feeding of High Fat and Fructose Diet (HFFD), there was an increase in the average body weight of rats in each group. The increase in body weight in rats is one of the effects of dyslipidemia conditions obtained through HFFD induction.⁴³ The highest weight gain was experienced by the white rice group (WR) at 26.3 grams, the positive control group (CP) at 25.3 grams, the analogue rice group (BAR) at 23.2 grams, and the smallest weight gain was experienced by the negative control group (CN) at 17.7 grams.

Result of Histopathological Observation of Kidney Damage

Kidney histopathological observations based on the damage score of glomerular cells and tubular cells are presented in the table of

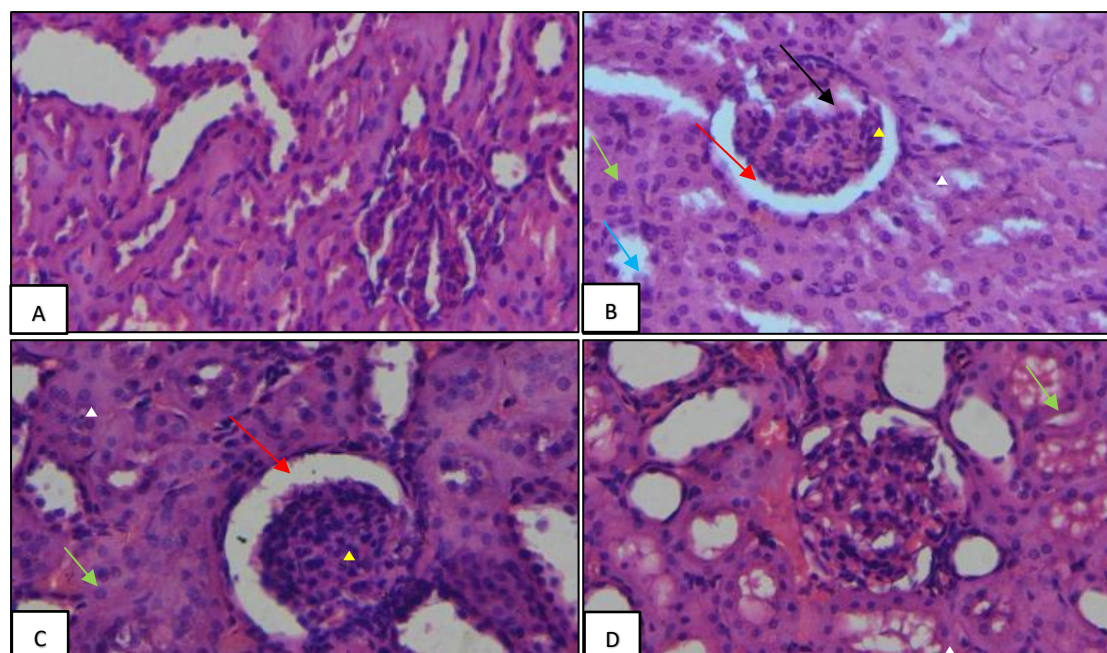
kidney histopathological damage score assessment results (Table 2). The glomerulus was given a score of 1 if there was inflammatory cell infiltration, score 2 if there was oedema in the bowman space, or score 3 if there were necrosis cells. Tubular cells are given a value of 1 if there is inflammatory cell infiltration, a value of 2 if there is edema of tubular epithelial cells, or a value of 3 if there are necrosis cells.⁴²

Observation of the histopathological picture of the kidneys was carried out by two observers, so it was necessary to test the reliability of the observation data with the Cronbach's Alpha test and obtained a $p > 0.6$ value which means the data is reliable. The histopathological picture of the kidney with 400x magnification is presented in Figure 1.

Table 2
Histopathological Score of Kidney Damage

Number of Samples	Histopathological Score of Kidney Damage			
	CN	CP	WR	BAR
1	2,6	4,7	5,5	3,7
2	3	5,3	5	3,5
3	2,6	5,6	5,7	3
4	1,8	5,4	5,6	3,6
5	1,1	5,4	4,5	3,3
6	2,7	5,5	5,8	2
Average	2,5	5,3	5,4	3,2

CN=Negative Control Group; CP=Positive Control Group; WR=White Rice Group; BAR=Banana-Based Analogue Rice Group



A=CN; B=CP; C=WR; D=BAR; Black arrows: inflammatory cell infiltration in the glomerulus; Red arrows: Bowman's chamber oedema; Yellow triangles: glomerular cell necrosis; Blue arrows: inflammatory cell infiltration in the tubules; Green arrows: tubular epithelial oedema; White triangles: tubular cell necrosis;

Figure 1
Result of Histopathological Observation of Kidney Damage

Table 3
Result of Post-Hoc Bonferroni Comparison Test of Histopathological Kidney Damage

Groups	Groups	p value
CN	CP	0.000*
	WR	0.000*
	BAR	0.077
CP	CN	0.000*
	WR	1.000
	BAR	0.000*
WR	CN	0.000*
	CP	1.000
	BAR	0.000*
BAR	CN	0.077
	CP	0.000*
	WR	0.000*

(*) = significance result of $p < 0.05$

Statistical Analysis of Histopathological Data of Kidney Damage

This study aims to see the effect of banana-based analogue rice on the histopathological picture of the kidneys with HFFD. The data in Table 2 were analyzed using One-Way ANOVA and showed a significance value of 0.000 ($p < 0.05$), indicating a significant difference in the histopathological features among the observed groups. Statical analysis was followed by Bonferroni Post-Hoc test to determine differences between the groups. The Bonferroni Post-Hoc test showed significant results when the p-value was less than 0.05 (Table 3).

Table 3 shows that significant differences ($p < 0.05$) between the CP and WR group with the CN group, considered normal, indicate damage to the kidney histopathology of the CP and WR groups. Significant differences ($p < 0.05$) were also seen between the BAR group given banana-based analog rice pellets with the CP and WR groups, indicating that giving banana-based analog rice to rats with dyslipidemia had an improvement effect on rat kidney damage. Meanwhile, insignificant differences ($p \geq 0.05$) were seen between the CP or dyslipidemia rats given standard pellets and the WR or dyslipidemia rats given white rice pellets, indicating that giving white rice did not improve rat kidney damage. Insignificant differences ($p \geq 0.05$) were also seen between the CN and the BAR group, indicating that kidney repair in BAR rats was close to the condition of the kidneys in normal rats.

DISCUSSION

The results showed that the negative control group (CN) had the lowest kidney histopathological damage score. This is because CN is a group that is given standard feed without induction of HFFD. Meanwhile, there was an increase in the score of renal histopathology damage in the group of rats with dyslipidemia or positive control (CP). The highest average score of kidney histopathological damage occurred in the white rice group (WR) of 5.4. The average score of kidney histopathological damage in the WR group increased higher than the CN group. The increase in kidney score value in the WR group is in line with previous research which shows that the kidneys of rats induced by High Fructose Diet for 40 days and streptozotocin (STZ) then fed with white rice pellets for 21 days have a glomerular damage score of 3 and a tubular damage score of 4. This value is greater than in the control group which has a glomerular and tubular damage score of 0.5 and 1.³⁰

The average score of kidney histopathology damage in the CP grup was also higher with a value of 5.3 compared to CN group of 2.3. This is in line with previous research which proves that the administration of HFFD for 14 days can trigger hypercholesterolemia to dyslipidemia marked by an increase in TG (mean TG level 145.32 ± 3.82 mg/dl) and a decrease in HDL (mean HDL level 25.10 ± 1.65 mg/dl).⁴⁴ The results of the damage score are also in line with previous research which observed

histopathological damage to the kidneys of rats with hypercholesterolemia, it was found that the average renal histopathological damage was higher in the group with hypercholesterolemia (mean cell necrosis 129.75 ± 3.59) compared to the normal group.⁴⁵ However, the scoring value of renal histopathological damage in the WR group was still higher than CP group. This can be due to the high GI value of white rice or white rice so that it can trigger an increase in blood sugar which is one of the factors in increasing total cholesterol, LDL, and TG levels which can worsen kidney damage.^{6,44}

Analysis with One-Way ANOVA test showed significant results with a value of $p < 0.05$. This is in accordance with the hypothesis in this study, namely the administration of banana-based analogue rice has an influence on the improvement of renal tissue histopathology compared to therapy without banana-based analogue rice in rats (*Rattus norvegicus*) induced by HFFD. Furthermore, the data were tested with Post-Hoc Bonferroni and showed significant results with a value of $p < 0.05$ in each CN and BAR group against CP and WR group. Whereas between CN and BAR group and between CP and WR group there was no significant difference ($p \geq 0.05$).

The results of the Bonferroni post-hoc analysis test showed that the difference between CN group and BAR group did not have a significant difference with a value of $p = 0.077$. The BAR group had a kidney histopathological damage score of 3.2 which was greater than the control group which was 2.3. This may be due to the analogue rice treatment in BAR which is one of the managements of dyslipidemia in the form of dietary improvement.²⁶ The improvement of the diet includes an increase in the nutritional profile of banana-based analogue rice such as rich in fibre, low GI, pectin compounds, and phenolics that provide hypocholesterolemic effects.³² So that it can have an improving effect on the kidney tissue of rats induced by HFFD. Meanwhile, the WR group with a damage score of 5.4 did not have a significant difference with CP group which had a value of 5.3. This may be due to the high GI in white rice (>70) which triggers an increase in blood sugar as one of the ballast factors in dyslipidemia.^{46,27}

The results of the significance difference between WR group and the BAR group are in line with research of Kumara, where rats with High

Fat Diet and STZ showed significant differences between the group given the white rice and the group given analogue rice with the significance value of glomerular and tubular damage respectively being $p = 0.003$ and $p = 0.002$.³⁰ The WR group had a damage score of 5.4 which was greater than BAR group with a damage score of 3.2. This is because the white rice has a high GI value (>70), which can increase blood sugar levels in plasma and trigger diabetes.⁴⁶ The increase in sugar levels results in an increase in the level of fat profile in the body whose complications can be cell damage to kidney tissue.^{6,18} The part of the kidney that when damaged can cause a decrease in function is in the functional unit or nephron, which is mainly the glomerulus and renal tubules.⁴⁷

The results of the Bonferroni Post-Hoc test also showed a significant difference between CP group and the BAR group with a p value of 0.000. This can be due to the banana content in analogue rice which has a hypocholesterolemic effect.³² The CP group had a kidney histopathological damage score of 5.3 which was greater than that of BAR group. This is related to dyslipidemia as one of the factors triggering the occurrence of CKD.²⁰

Banana-based analogue rice has a high fibre content so that it can increase the binding of bile acids which results in a decrease in blood cholesterol.³³ When high-fibre intake enters the digestive tract, fibre will bind bile acids in the intestinal lumen, so that bile acids cannot be absorbed into the liver. The liver, which requires bile acids in its metabolism, will use cholesterol in the blood to produce bile acids, so that cholesterol in the blood will decrease. Meanwhile, bile acids bound with fibre will be excreted through the faeces.⁴⁸ The low GI value of analogue rice allows an increase in short chain fatty acids (SCFA).⁴⁹ This was proven to reduce cholesterol levels by 17% in rats given butyrate for six weeks.⁵⁰

Banana-based analogue rice contains bananas which have pectin components that can help bind and reduce cholesterol absorption in the digestive tract.³³ Pectin has a mechanism similar to statin drugs, namely by inhibiting the HMG-CoA reductase enzyme, so that LDL receptors on the liver surface increase and attract LDL back to the liver.^{51,52}

Increased levels of lipid profiles in dyslipidemia will increase the secretion of

proinflammatory cytokines such as IL-6 and TNF- α , so that ROS will be triggered to increase. The increase in ROS can result in kidney tissue damage.^{53,54} This can be inhibited by phenolics, which are antioxidant compounds contained in bananas in analogue rice that can reduce ROS in less than one week.⁵⁵ The ability of phenolics as antioxidant compounds is due to the presence of phenol groups that can bind to a free radical by donating hydrogen atoms through an electron transfer process, so that phenolics turn into phenoxyl radicals. The phenoxyl radical formed will stabilise itself through the resonance effect.⁵⁶ Inhibition of ROS by phenolics results in damage to kidney tissue which is triggered by worsening not continuing in cell hypoxia which results in necrosis.³³

CONCLUSION

Based on the research that has been done, it can be concluded that there is an effect of giving banana-based analogue rice on the histopathological picture of the kidneys in rats (*Rattus norvegicus*) with HFFD. This is evidenced in the banana-based analogue rice group (BAR) has a 60 percent smaller kidney damage scoring value and a significant difference ($p=0.000$) compared to the positive control group (CP) and the white rice group (WR).

RECOMMENDATION

Future research can be performed by considering the termination and serial necropsy of kidney organs in order to assess the progressivity of kidney tissue damage. Statin treatment either alone or in combination with banana-based analogue rice may also be used to assess the effectiveness of banana-based analogue rice compared to current treatments.

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REFERENCES

1. Singgih I, Yustisia I, Santoso A, Aminuddin A, Kurniawan LB, Kasim H. Efek Pemberian High Fat and Fructose Diet (HFFD) dan Carbon tetrachloride (CCL4) Terhadap Kadar Cystatin Serum. *Indonesian Journal of Human Nutrition*. 2021;8(2):120–8. doi:10.21776/ub.ijhn.2021.008.02.3
2. Mustakim, Munir, Irmayani. Warna dan Indeks Kuning Telur Puyuh (*Coturnix japonica*) yang diberi Tepung Daun Singkong (*Manihot asculenta*) dengan Level yang Berbeda. *Jurnal Gallus-Gallus*. 2023;1(3):2985–640. doi:10.51978/gallusgallus.v1i3.362
3. Nurfianti A, Tribudi YA. Kadar Malondialdehid (MDA) dan Kolesterol pada Telur Puyuh yang diberi Pakan Tambahan Tepung Pegagan (*Centella asiatica*). *Jurnal Teknologi Pertanian*. 2016;17(3):187–94. doi:10.21776/ub.jtp.2016.017.03.4
4. Puglisi MJ, Fernandez ML. The Health Benefits of Egg Protein. *Nutrients*. 2022;14(14). doi:10.3390/nu14142904
5. Zhao B, Gan L, Graubard BI, Männistö S, Albanes D, Huang J. Associations of Dietary Cholesterol, Serum Cholesterol, and Egg Consumption With Overall and Cause-Specific Mortality: Systematic Review and Updated Meta-Analysis. *Am Hear Assoc*. 2022;145(20):1506–20. doi:10.1161/circulationaha.121.057642
6. Susanti N, Rahmawati E, Kristanti RA. Efek Diet Tinggi Fruktosa terhadap Profil Lipid Tikus *Rattus Rattus norvegicus* Strain Wistar. *J Islam Med*. 2019;3(2):26–35. doi:10.18860/jim.v3i2.8724
7. Liwanto G, Santoso AH. Hubungan Asupan Gula Dalam Minuman Bersoda Dengan Obesitas Pada Mahasiswa Fakultas Kedokteran Universitas Tarumanagara. *J Muara Med dan Psikol Klin*. 2021;1(1):1. doi:10.24912/jmmpk.v1i1.12050
8. Permenkes. Permenkes No. 30 Th 2013. 2013.
9. Cahyani AAAE, Santosa B, Mukaromah AH. Pengaruh Pemberian Variasi Konsentrasi Biotin Terhadap Kadar Kolesterol Total Resiko Dislipidemia. *Bali Med J*. 2022;9(1):1–10. doi:10.36376/bmj.v9i1
10. Elhaq IH, Ramdhan DH. Analisis Faktor Risiko Dislipidemia Karyawan Kantor PT. X di Jakarta Tahun 2022. *J Keselam Kesehat Kerja dan Lingkung*. 2024;5(1):76–82. doi:10.25077/jk3l.5.1.76-82.2024
11. Mohamed-Yassin MS, Baharudin N, Abdul-Razak S, Ramli AS, Lai NM. Global prevalence of dyslipidaemia in adult populations: A systematic review protocol. *BMJ Open*. 2021;11(12):9–12. doi:10.1136/bmjopen-2021-

- 049662
12. Nasution AA, Siregar PP, Nasution YA. Laporan Kunjungan Rumah Kasus Dislipidemia : pengalaman mahasiswa kedokteran stase Kesehatan Komunitas. *J Implementasi Husada*. 2022;2(3):266–72. doi:10.30596/jih.v2i3.11488
 13. Tobias DK. What Eggsactly Are We Asking Here? Unscrambling the Epidemiology of Eggs, Cholesterol, and Mortality. *Am Hear Assoc*. 2022;145(20):1521–3. doi:10.1161/circulationaha.122.059393
 14. Permenkes. Permenkes No. 28 Tahun 2019. 2019
 15. Santya T, Suharyanto CE, Simanjuntak P, Alfandianto A. Sistem Pakar Menentukan Maksimal Kalori Harian Berbasis Mobile. *Innov Res Informatics*. 2019;1(2):70–7. doi:10.37058/innovatics.v1i2.920
 16. Sutanto K, Karjadijaja I. Hubungan antara Obesitas Sentral dengan Kejadian Dislipidemia pada Karyawan Universitas Tarumanagara Pengunjung Poliklinik Fakultas Kedokteran Universitas Tarumanagara November 2016 - April 2017. *Tarumanagara Med J*. 2019;1(2):352–60. doi:10.24912/TMJ.V1I2.3836
 17. Haile K, Timerga A. Dyslipidemia and its associated risk factors among adult type-2 diabetic patients at jimma university medical center, Jimma, Southwest Ethiopia. *Diabetes, Metab Syndr Obes*. 2020;13:4589–97. doi:10.2147/DMSO.S283171
 18. Rifat ID, Hasneli N Y, Indriati G. Gambaran Komplikasi Diabetes Melitus Pada Penderita Diabetes Melitus. *J Keperawatan Prof*. 2023;11(1):52–69. doi:10.33650/jkp.v11i1.5540
 19. Kathak RR, Sumon AH, Molla NH, Hasan M, Miah R, Tuba HR, et al. The association between elevated lipid profile and liver enzymes: a study on Bangladeshi adults. *Sci Rep*. 2022;12(1):1–8. doi:10.1038/s41598-022-05766-y
 20. Purqoti DN, Arifin Z, Fatmawati BR, Ilham I, Istianah I, Hapipah H. Upaya Pengenalan Faktor Risiko Dan Pencegahan Gagal Ginjal Kronis. *LOSARI J Pengabdian Kpd Masy*. 2023;5(1):6–10. doi:10.53860/losari.v5i1.118
 21. Shu S, Wang Y, Zheng M, Liu Z, Cai J, Tang C, et al. Hypoxia and hypoxia-inducible factors in kidney injury and repair. *Cells*. 2019;8(3):1–21. doi:10.3390/cells8030207
 22. Dong XQ, Chu LK, Cao X, Xiong QW, Mao YM, Chen CH, et al. Glutathione Metabolism Rewiring Protects Renal Tubule Cells Against Cisplatin-Induced Apoptosis and Ferroptosis. *Redox Rep*. 2023;28(1). doi:10.1080/13510002.2022.2152607
 23. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular Disease in Chronic Kidney Disease Pathophysiological Insights and Therapeutic Options. *Circulation*. 2021;143(11):1157–72. doi:10.1161/circulationaha.120.050686
 24. Portolés J, Martín L, Broseta JJ, Cases A. Anemia in Chronic Kidney Disease: From Pathophysiology and Current Treatments, to Future Agents. *Front Med*. 2021;8(March):1–14. doi:10.3389/fmed.2021.642296
 25. Shroff R, Wesseling-Perry K, Bacchetta J. Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD). *Pediatr Nephrol Eighth Ed*. 2022;52(1):1751–78. doi:10.1007/978-3-030-52719-8_129
 26. Nuswantoro A, Aprillia D, Juliana Cristyaningsih. Lipid Profile of Prolanis Patients in Pontianak City. *J Teknol Kesehat Borneo*. 2023;4(1):1–9. doi:10.30602/jtkb.v4i1.209
 27. Wari AT, Muhlishoh A, Nurzihan NC. Indeks Glikemik Dan Beban Glikemik Makanan Kaitannya Dengan Kadar Ldl Dan Rlpp Pasien Diabetes Mellitus Tipe-2. *J Nutr Coll*. 2023;12(1):61–9. doi:10.14710/jnc.v12i1.36164
 28. Wijonarko W, Ferry F. Identification and management of chronic kidney disease: A case study. *Holistik J Kesehat*. 2024;18(2):233–9. doi:10.33024/hjk.v18i2.108
 29. Sumardiono S, Budiyo B, Kusumayanti H, Silvia N, Luthfiani VF, Cahyono H. Production and physicochemical characterization of analog rice obtained from sago flour, mung bean flour, and corn flour using hot extrusion technology. *Foods*. 2021;10(12). doi:10.3390/foods10123023
 30. Kumara PP, Hairrudin, Normasari R. Beras Analog dapat Mencegah Kerusakan Ginjal pada Tikus Induksi Kombinasi HFD dan STZ. *Indones J Hum Nutr*. 2021;8(1):8–20. doi:10.21776/ub.ijhn.2021.008.01.2
 31. Rachman A, Brennan MA, Morton J, Brennan CS. Effect of cassava and banana flours blend on physico-chemical and glycemic characteristics of gluten-free pasta. *J Food Process Preserv*. 2019;43(9):1–8. doi:10.1111/jfpp.14084
 32. Kusumawardani HD, Marsono Y, Murdiati A, Samsudin M. Potensi Tepung Pisang Uter (Musa Acuminata) Sebagai Pangan Fungsional Untuk Menurunkan Kolesterol. *Bul Penelit Kesehat*. 2020;47(4):275–82. doi:10.22435/bpk.v47i4.1589
 33. Prameswari DC. Konsumsi Pisang dalam Menurunkan Kadar Kolesterol Darah. *J Penelit Perawat Prof*. 2021;3(3):511–8. doi:10.37287/jppp.v3i3.537
 34. Zahra NI, Siregar PP. Perilaku Konsumsi Serat Pada Mahasiswa Angkatan 2020 Fakultas Kesehatan Masyarakat Universitas Islam Negeri

- Sumatera Utara Tahun 2023. *JK J Kesehat.* 2023;1(1):177–85.
35. Falcomer AL, Riquette RFR, De Lima BR, Ginani VC, Zandonadi RP. Health benefits of green banana consumption: A systematic review. *Nutrients.* 2019;11(6):1–22. doi:10.3390/nu11061222
 36. K. Netshiheni R, O. Omolola A, A. Anyasi T, I.O. Jideani A. Banana Bioactives: Absorption, Utilisation and Health Benefits. *Banan Nutr - Funct Process Kinet.* 2020. doi:10.5772/intechopen.83369
 37. Horne RG, Yu Y, Zhang R, Abdalqadir N, Rossi L, Surette M, et al. High fat-high fructose diet-induced changes in the gut microbiota associated with dyslipidemia in Syrian hamsters. *Nutrients.* 2020;12(11):1–20. doi:10.3390/nu12113557
 38. Arifin WN, Zahiruddin WM. Sample Size Calculation in Animal Studies Using Resource Equation Approach. *Malaysian J Med Sci.* 2017;24(5):101–5. doi:10.21315/mjms2017.24.5.11
 39. Octavia ZF, Widyastuti N. Pengaruh Pemberian Jus Daun Ubi Jalar (*Ipomoea batatas* (L.) Lam) Terhadap Kadar Trigliserida Tikus Wistar Jantan (*Rattus norvegicus*) yang Diberi Pakan Tinggi Lemak. *J Nutr Coll.* 2014;3(4):838–47. doi:10.21315/mjms2017.24.5.11
 40. Ghasemi, Asghar; Sajad JKK. Review article : The Laboratory Rat: Age and Body Weight Matter. *EXCLI J.* 2021;2005:1431–45. doi:10.17179/excli2021-4072
 41. Kurniasari I, Kusnandar F, Budijanto S. Karakteristik Fisik Beras Analog Instan Berbasis Tepung Jagung dengan Penambahan k-Karagenan dan Konjak. *agriTECH.* 2020;40(1):64. doi:10.22146/agritech.47491
 42. Mustofa S, Dewi SN. *Rhizophora apiculata* Bark Ethanolic Extracts Prevent Kidney Damage Caused by Cigarette Smoke in Male Rats. *Sriwij J Med.* 2023;6(1):17–23. doi:10.32539/sjm.v6i1.204
 43. Gilles CF coudray, Claire F, Béatrice V, Bernard B, Blachnio-zabielska A, Rieusset J, et al. Long-Term Measures of Dyslipidemia , Inflammation , and Oxidative Stress in Rats Fed a High-Fat / High-Fructose Diet. *Lipids.* 2019;54(1):81-97. doi:10.1002/lipd.12128
 44. Rahmawati FC, Djamiatun K, Suci N. Pengaruh yogurt sinbiotik pisang terhadap kadar glukosa dan insulin tikus sindrom metabolik. *Jurnal Gizi Klinik Indonesia.* 2017;14(1):10–8. doi:10.22146/ijcn.19379
 45. Fauziah, Febriani H, Rahmadina. Uji Aktivitas Ekstrak Daun Samarinda (*Carissa carandas* L.) Terhadap Histopatologi Ginjal Tikus Putih (*Rattus norvegicus* L.) Hiperkolesterolemia. *Biol Educ Sci Technol.* 2021;4(2):339–45. doi:10.30743/best.v4i2.4544
 46. Ali A, Waly MI, Al-Mahrazi M, Al-Maskari J, AlWaheibi S. Glycemic Index and Glycemic Load of Selected Omani Rice Dishes. *Food Sci Eng.* 2022;4(1):1–8. doi:10.37256/fse.4120231858
 47. Fattah H, Layton A, Vallon V. How Do Kidneys Adapt to a Deficit or Loss in Nephron Number? *Physiology.* 2019;34(3):189–97. doi:10.1152/physiol.00052.2018
 48. Sinulingga BO. Pengaruh konsumsi serat dalam menurunkan kadar kolesterol. *J Penelit Sains.* 2020;22(1):9–15. doi:10.26554/jps.v22i1.556
 49. Yoeantafara A, Martini S. Pengaruh Pola Makan Terhadap Kadar Kolesterol Total (The Influence of Diet to Total Cholesterol Levels). *J MKMI.* 2017;13(4):304–9. doi:10.30597/mkmi.v13i4.2132
 50. Feng Y, Xu D. Short-chain fatty acids are potential goalkeepers of atherosclerosis. *Front Pharmacol.* 2023;14:1–10. doi:10.3389/fphar.2023.1271001
 51. Azqinar TC, Anggraini DI, Kania S. Penatalaksanaan Holistik Pada Wanita Usia 60 Tahun dengan Dislipidemia Melalui Pendekatan Kedokteran Kekeluargaan. *J Penelit Perawat Prof.* 2022;4:1093–100. doi:10.37287/jppp.v4i4.1105
 52. Oktavelia W, Kusuma SAF. Therapy for Dyslipidemia: Plant Inhibitors of HMG-CoA Reductase. *Indones J Biol Pharm.* 2022;2(3):159–70. doi:10.24198/ijbp.v2i3.41376
 53. Düsing P, Zietzer A, Goody PR, Hosen MR, Kurts C, Nickenig G, et al. Vascular Pathologies in Chronic Kidney Disease: Pathophysiological Mechanisms and Novel Therapeutic Approaches. *J Mol Med.* 2021;99(3):335–48. doi:10.1007/s00109-021-02037-7
 54. Ayunda RD, Malita S. Pemanfaatan Senyawa Flavonoid sebagai Antioksidan pada Penderita Hiperkolesterolemia : Studi Literatur. *J Kedokt Unram.* 2024;13(3). doi:10.29303/jk.v13i3.5388
 55. Świetek M, Lu YC, Konefal R, Ferreira LP, Cruz MM, Ma YH, et al. Scavenging of Reactive Oxygen Species by Phenolic Compound-Modified Maghemite Nanoparticles. *Beilstein J Nanotechnol.* 2019;10:1073–88. doi:10.3762/BJNANO.10.108
 56. Asih DJ, Kadek Warditiani N, Wiarsana IGS. Review Artikel: Aktivitas Antioksidan Ekstrak Amla (*Phyllanthus emblica/Emblca officinalis*). *J Ilm Multidisplin Indones.* 2022;1(6):674–87. doi:10.32670/ht.v1i6.1533