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ORIGINAL ARTICLE

The effect of binahong leaf extract on cardiac function in rats fed a high-fat diet

Dwi Sukma Wahyudi[1], Dewi Sartika[2], Alvin Abrar Harahap[3]*

Abstract

Several antioxidant defense mechanisms protect biological systems from the negative impact of ROS. Natural antioxidants are mainly obtained from plants, such as vegetables, and one of them is the binahong plant which is rich in antioxidants. This plant is often used traditionally as a blood-thinning drug to prevent stroke. This study aimed to evaluate the effect of binahong (anderera cardifolia) leaf extract on cardiovascular health and the histological structure of the heart of wistar male white rats fed a high-fat diet. This study is an experiment with a completely randomized design (CRD) consisting of 4 groups: normal control, treatment 1 dose 200 mg/kg BW, treatment 2 dose 300 mg/kg BW, and treatment 3 dose 400 mg/kg BW. Histopathological data such as aortic wall thickness and number of foam cells were analyzed using SPSS 23 with one-way ANOVA test and Post Hoc LSD at 0.05 significance level. The results showed that administering a dose of 400 mg/kg BW effectively reduced the thickness of the aortic wall and the number of aortic foam cells in rats.

Keywords: binahong leaf extract, heart, histopathology

Introduction

The quantity and quality of food consumed significantly affect human health.[1] Eating habits are closely linked to well-being, making it essential to consume all necessary nutrients in appropriate amounts to maintain a balanced diet and good health.[2] One key recommendation for a healthy diet is the consumption of vegetables and fruits. Unfortunately, in Indonesia, only 63.3% of the population meets the recommended intake of fruits and vegetables. This deficiency contributes to increased body mass index (BMI), raising the risk of overweight and obesity.[3]

Obesity is characterized by an imbalance between weight and height, primarily caused by excessive fat accumulation. It is considered a global pandemic and is associated with numerous non-communicable chronic diseases, including metabolic syndrome, type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), obstructive sleep apnea, osteoarthropathy, and certain cancers.[4] Obesity is a serious issue that affects all age groups, from children to adults. The condition should not be underestimated, as it can lead to severe effects on vital organs, beyond merely causing excessive weight and lethargy.[5] The primary cause of obesity is energy imbalance, where energy intake exceeds expenditure. Excessive energy intake is a key driver of weight gain. The quality of food intake also influences energy balance through complex hormonal and neurological pathways that regulate satiety and potentially other mechanisms.[6] Globally, obesity has been proven to be a significant risk factor for CVD. It is often associated with hypertension, dyslipidemia,

Affiliation
[1]Master's Programme in Biomedical Sciences, Universitas Prima Indonesia
[2]Departement of Nursing, Universitas Prima Indonesia
[3]Departement of Clinical Medicine, Universitas Prima Indonesia

Correspondence
alvinabrarharahap@unprimdn.ac.id

diabetes, or insulin resistance, as well as elevated fibrinogen and C-reactive protein levels, all of which increase the risk of CVD events.[7,8]

Cardiovascular disease (CVD) is the leading cause of death worldwide and a significant contributor to disability and reduced quality of life.[9] CVD refers to diseases affecting the heart or blood vessels (the cardiovascular system).[10] The cardiovascular system is critical in transporting nutrients, oxygen, and immune system components throughout the body. Through the hemostatic system, the body maintains the integrity of blood vessels and prevents bleeding. Biochemical and physical processes governing circulation interact over vast temporal and spatial scales, ranging from cellular functions to large-scale blood flow structures. Dysfunction in the heart or circulatory system can result in severe consequences. As a heterogeneous group of conditions, CVD accounts for a significant number of global deaths.[11] The cardiovascular system supplies blood to the entire body and adapts to various stimuli to regulate the flow and volume of blood through the vessels. It comprises the heart, arteries, veins, and capillaries. The heart and blood vessels work intricately to ensure adequate blood flow to all body regions. Numerous factors, including blood volume, hormones, electrolytes, osmolarity, medications, adrenal glands, kidneys, and more, influence regulation of the cardiovascular system. The parasympathetic and sympathetic nervous systems also play a pivotal role in cardiovascular regulation. The primary function of the heart is to pump blood throughout the body. In a healthy state, the muscular heart performs two main tasks. First, it draws oxygen-depleted blood from tissues and pumps it to the lungs, where oxygen is absorbed, and carbon dioxide is expelled. Second, the heart takes oxygen-rich blood from the lungs and distributes it to the rest of the body. Additionally, the heart removes interstitial fluid from the bloodstream and transports it to the extracellular space through systemic circulation..[12]

The heart's primary function is to pump blood throughout the body, serving as the central unit of the cardiovascular system.[13] In a healthy state, the heart performs two critical tasks. First, it draws oxygen-depleted blood from the tissues and pumps it to the lungs, where oxygen is absorbed, and carbon dioxide is expelled. Second, it delivers oxygen-rich blood from the lungs to the rest of the body. Additionally, the heart removes interstitial fluid from the bloodstream and transports it to the extracellular space through systemic circulation.[14]

The pathophysiology of cardiovascular diseases (CVD), primarily caused by atherosclerosis, includes vascular remodeling that restricts blood flow, affecting both the heart and the nervous system.[15] Aging is another significant risk factor, as it increases the prevalence of CVD due to the accumulation of oxidative damage. Oxidative stress, a key contributor to the development of CVD, arises when reactive oxygen species (ROS) production exceeds the body's antioxidant capacity.[16] ROS are byproducts of mitochondrial respiration or metabolism and are also produced by specific enzymes. Environmental factors such as ultraviolet exposure, radiation, smoking, and excessive alcohol consumption exacerbate ROS production, contributing to pathologies like cancer and CVD.[17] Global evidence suggests that up to 90% of CVD cases can be prevented by controlling modifiable risk factors, such as adopting a diet rich in antioxidants.[18] Natural antioxidant sources are primarily plant-based, including vegetables, fruits, spices, and herbs, abundant in vitamins, phenolic compounds, carotenoids, and trace elements.[19] Antioxidants function by delaying or preventing the oxidation of other molecules.[20]

One plant rich in antioxidants is binahong (Anredera cordifolia). Binahong, known by its regional names in Indonesia, belongs to the Basellaceae family and originates from the Americas. It is a climbing plant that can grow up to approximately 5 meters long.[21] It has rhizome roots, soft cylindrical stems, reddish coloration, and green leaves arranged alternately on the stem. At three years of age, the plant forms tubers or rough-textured rhizomes. It thrives in tropical and subtropical climates.[22] Phytochemical screening of binahong indicates the presence of saponins, steroids/terpenoids, flavonoids, alkaloids, and tannins.[23] This study aims to investigate the effect of binahong leaf extract on cardiac function and the histopathological features of the heart in male Wistar rats fed a high-fat diet.

Method

Study Design and Sampling

This study employed a post-test only group design to evaluate the effects of binahong leaf extract (Anredera cordifolia) on cardiac function and histopathological features of the heart in male Wistar rats

(Rattus norvegicus) fed a high-fat diet. Male Wistar rats aged 2–3 months and weighing 160–200 g were selected due to their physiological similarities to humans. Inclusion criteria included healthy rats with no anatomical abnormalities, while exclusion criteria involved rats that died or developed defects during the experiment. Sample size was calculated using the Federer formula, resulting in 24 rats divided into four groups randomly.

Tools and Material

Tools included rat cages, Ohaus scales, glass jars, rotary evaporator, blender, stirrer, porcelain dishes, test tubes, stopwatch, 3 mL syringes, gloves, masks, blunt-ended sond needles, blood capillary pipettes, spectrophotometer, HDL and LDL quantitation kits, precipitation buffer, enzymatic colorimetric kits, hematocrit pipettes, and Eppendorf tubes. Materials included rat feed and water, binahong leaves, ethanol (96%), formalin (10%), NaCl, graded alcohol (70%, 80%, 90%), xylol, paraffin, HE staining reagents, and adhesives.

Preparation of Binahong Leaf Extract

Binahong leaves were washed, dried, and ground into powder. The powder was extracted using 96% ethanol, filtered, and evaporated with a rotary evaporator.

Animal Preparation

Rats were fed a high-fat diet for 14 days using duck egg yolks as the primary source of fat and protein. Obesity was determined by the Lee index (>0.300). After acclimation and diet administration, the treatment phase began.

Treatment Procedure

After acclimation and high-fat feeding, the rats were randomly divided into four groups, each consisting of six rats. Groups included a control group (administered distilled water) and three treatment groups receiving binahong leaf extract in different dosages. Rats were labeled using waterproof markers on their tails. After 14 days of treatment, the rats were terminated under anesthesia, and their hearts were collected for analysis. The remaining rats were buried post-experimentation.

Cardiac Function Assessment

Cardiac biomarkers, particularly troponin T (TnT), were measured to assess cardiac stress or damage. Blood samples (3 cc) were collected from the orbital vein on day 15 using a capillary pipette, stored in EDTA tubes, and kept in a cool box. The TnT levels were analyzed using a Troponin-T Cardiac Reader (Roche Diagnostics).

Histopathological Preparations

On day 14, necropsy was performed under chloroform anesthesia. The hearts were fixed in 10% formalin solution and sent to the Laboratory of Universitas Sumatera Utara for histological processing. Tissue samples were stained with Hematoxylin and Eosin (HE) and examined under a microscope.

Histopathological Observations

Damage levels were classified into four grades: a) Grade 0: No damage; b) Grade 1: 0–30% damage; c) Grade 2: 30–60% damage; and d) Grade 3: >60% damage. Damage markers included inflammation or inflammatory cell infiltration in the myocardium and eosinophilia in the cytoplasm of myocardial cells.

Data Analysis

Histopathological data were scored, tabulated, and analyzed descriptively using SPSS 25.0. Normality was tested with the Kolmogorov-Smirnov test, while significance between groups was determined using One-Way ANOVA at a 95% confidence level. Post Hoc analysis was conducted using the LSD technique to identify specific group differences.

Results

In this study, observations were made on the body weight of white rats to determine the effect of binahong leaf extract on rats fed a high-fat diet. It can be seen that the analyzed group data showed normal distributed data results through the *Shapiro Wilk test* ($p > 0.05$). The homogeneous test was carried out by *the Levenne* test ($p > 0.05$). In the post-cholesterol induction group, it was seen that the normal group had a body weight of 223.00 grams. In the post-cholesterol induction treatment group, it was seen that P1 had a body weight of 289.25 grams, P2 had a body weight of 269.25 grams, and P3 had a body weight of 272.25 grams. In body weight after being fed a high-fat diet, there was an increase in P3 followed by P2, P1, and K. In the post-extract group, it was seen that group K had a body weight of 235.50 grams. In the post-extraction treatment group, it was seen that P1 had a body weight of 275.75 grams, P2 had a body weight of 254.00 grams, and P3 had a body weight of 268.25 grams. In body weight after being given binahing leaf extract, there was weight loss in the P1, P2, and P3 groups. and the control group experienced weight gain.

Table 1. Body weight during high-fat diet induction and post-extract treatment

Group Treatments	Parameter (Average (gram) ± SD)	
	BB Induction High-Fat Diet (g)	BB Post Extract
K	224,00 ± 1,82[b]	235,50 ± 2,08[a]
P_1	289,25± 2,50[e]	275,75 ± 3,09[f]
P_2	269,25 ±1,89[d]	254,00 ± 0,82[d]
P_3	272,25 ±1,70[d]	268,25 ± 2,23[e]

Explanation: SD : Standard Deviation, abcdef : Letters indicating significant differences ($p < 0.05$),BB : Body Weights, K : Control, P_1 : Dosage 200 mg/kg BB, P_2 : Dosage 300 mg/kg BB, P_3 : Dosage 400 mg/kg BB

Table 2. Aortic wall thickness

Group Treatments	Parameter (Rata-Rata (µm)±SD)
	Aortic Wall Thickness
K+	75,35 ± 1,87[b]
P_1	93,00 ± 1,67[d]
P_2	88,77 ± 1,28[c]
P_3	88,00 ± 2,26[c]

The administration of a high-fat diet at a dose of 3 mL/200 grams of body weight over 14 days led to weight gain in rats in groups P1, P2, and P3, while the control group did not experience any weight increase. Differences in body weight among the rats may be attributed to variations in individual physiological responses. Factors such as handling during the study, blood sampling, weighing, caging, and cleaning of cages could have induced stress, affecting their body weight. Widyaningsih & Salamah[24] stated that there was no significant difference in weight gain among the groups following the high-fat diet. This may be due to stress, excessive physical activity, and other factors.

The administration of binahong leaf extract at doses of 200 mg/kg, 300 mg/kg, and 400 mg/kg body weight for two weeks showed no significant effect in reducing the body weight of the rats. Groups P1, P2, and P3 showed weight gain, while the control group exhibited weight loss. This suggests that different doses of binahong leaf extract did not influence weight reduction, and similarly, the high-fat diet did not lead to weight gain in the control group. Research indicates that overweight (obesity) is associated with higher blood pressure compared to normal weight. Weight gain is closely linked to the accumulation of fat (plaque) in the body, which forces the heart to work harder to pump blood. This occurs due to the buildup of plaque in blood vessels. However, elevated blood pressure can also occur in individuals with normal body weight due to factors such as age, dietary habits, physical inactivity, and others.

The average aortic wall thickness was measured as 75.35 µm in the control group (K+), 93.00 µm in group P1, 89.77 µm in group P2, and 88.00 µm in group P3. These values indicate that the oral medication and binahong extract treatments affected a reduction in aortic wall thickness. The control group demonstrated the most significant impact on reducing aortic wall thickness compared to groups P1, P2, and P3. Among the treatment groups, P3, which received the highest dose (400 mg/kg body weight), showed the lowest value of aortic wall thickness at 88.00 µm. This indicates that the 400 mg/kg BB dose had the most substantial effect on reducing aortic wall thickness. A study by Wibowo [25] reported the normal aortic thickness in rats to be approximately 71 µm. This suggests that the reduction observed in group P3 brings the aortic wall thickness closer to the normal range, highlighting the efficacy of the highest dose of binahong leaf extract in this study.

In Figure 1, the aortic wall thickness of Wistar rats in the control group (without high-fat diet induction) displayed normal aortic layers with no protrusions in the tunica intima and tunica media. The aorta is composed of three layers: the tunica intima, tunica media, and tunica adventitia. In a normal aorta, the tunica intima consists of a single layer of endothelial cells and subendothelial connective tissue. The

tunica media contains abundant elastic fibers and smooth muscle cells, separated from the tunica intima by a dense elastic membrane known as the internal elastic lamina.[26]

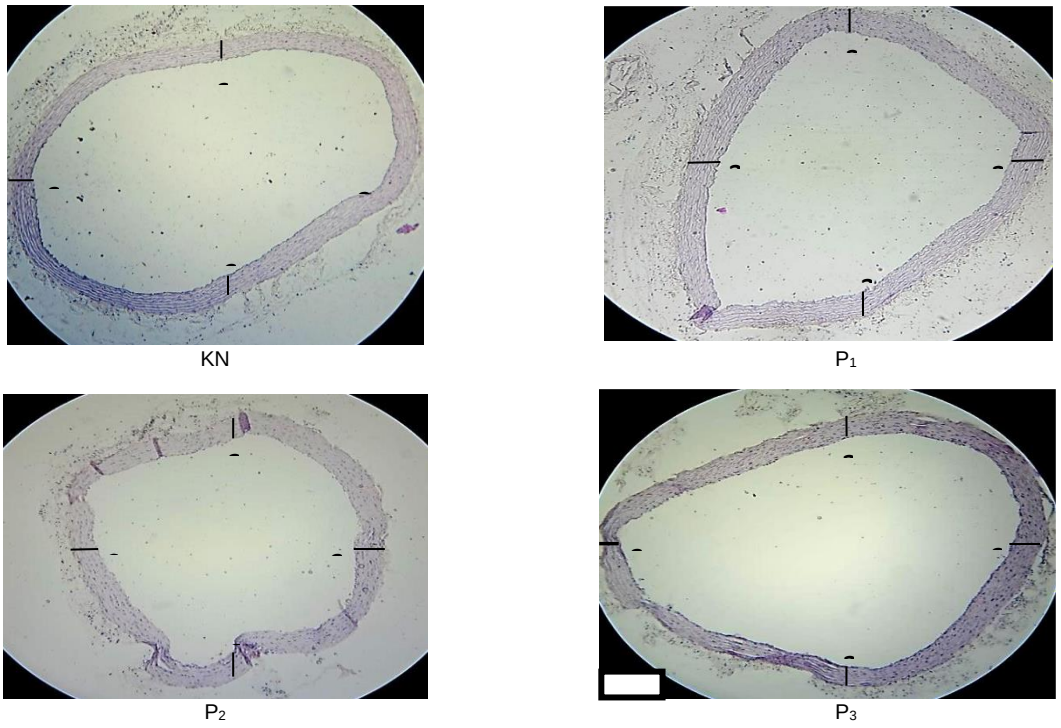

Figure 1. Thickness of the Cardiac Aortic Wall in Each Group (100x Magnification)

In groups P1, P2, and P3, protrusions indicating fat accumulation in the tunica intima and media were observed. Fat accumulation begins with the formation of atherosclerotic plaques. Atherosclerosis is the buildup of plaques in the inner walls of arteries, which leads to arterial thickening and narrowing of the lumen, thereby disrupting blood circulation to target organs, such as the myocardium.[27] In this study, the most effective treatment in reducing aortic wall thickness was observed in group P3, which received a 400 mg/kg BW dose of binahong leaf extract. Groups P1 and P2 showed less pronounced effects. The effectiveness of the extract is attributed to the presence of antioxidant compounds, particularly flavonoids, in binahong leaves. Flavonoids scavenge free radicals and improve endothelial function, thereby contributing to vascular repair and reducing aortic wall thickness.

This study observed the number of foam cells to assess the effects of binahong leaf extract on the aorta of hypercholesterolemic rats. The data showed that the average number of foam cells varied across groups. The average aortic wall thickness in the control group was 0.55, while the values in groups P1, P2, and P3 were 1.70, 1.40, and 1.30, respectively. The control group had the lowest average value.

Table 3. Number of Foam Cells

Group Treatments	Parameter (Average (µm)±SD) Number of Foam Cells
K+	0,55± 0,30[a]
P_1	1,70± 0,28[b]
P_2	1,40± 0,34[b]
P_3	1,30± 0,18[a]

The treatment groups (P1, P2, and P3) demonstrated a reduction in the number of foam cells, with the control group showing a more significant effect compared to the treatment groups. Among the treatment groups, P3 had the lowest value, indicating that a dose of 400 mg/kg BW was effective in reducing foam cell numbers. Previous research (Fikriah, 2005) reported that the normal average number of foam cells in rats is approximately 1 µm. The reduction in foam cell numbers observed in group P3 suggests that this dose brings the value closer to the normal range for rat aortas.

In Figure 2, it can be seen that the number of foam cells in the aorta of white rats of the KN group without induction of high-fat feed shows a normal layer of aorta that is neatly arranged, there are no foam cells in tunica intima and tunica media. In the control group, it was seen that the number of foam cells in tunica intima and tunica media was due to the induction of high-fat feed. In the P1, P2 and P3 groups, the

number of foam cells in the aorta can be seen to be only small compared to the control group. The most effective extract treatment in reducing the number of foam cells was found in the P3 group with an extract dose of 400 mg/kg BB. This is because in binahong there are flavonoid compounds that play a role in lowering cholesterol, triglycerides, LDL levels and increasing HDL levels and inhibiting the formation of foam cells so that early lesions do not occur.

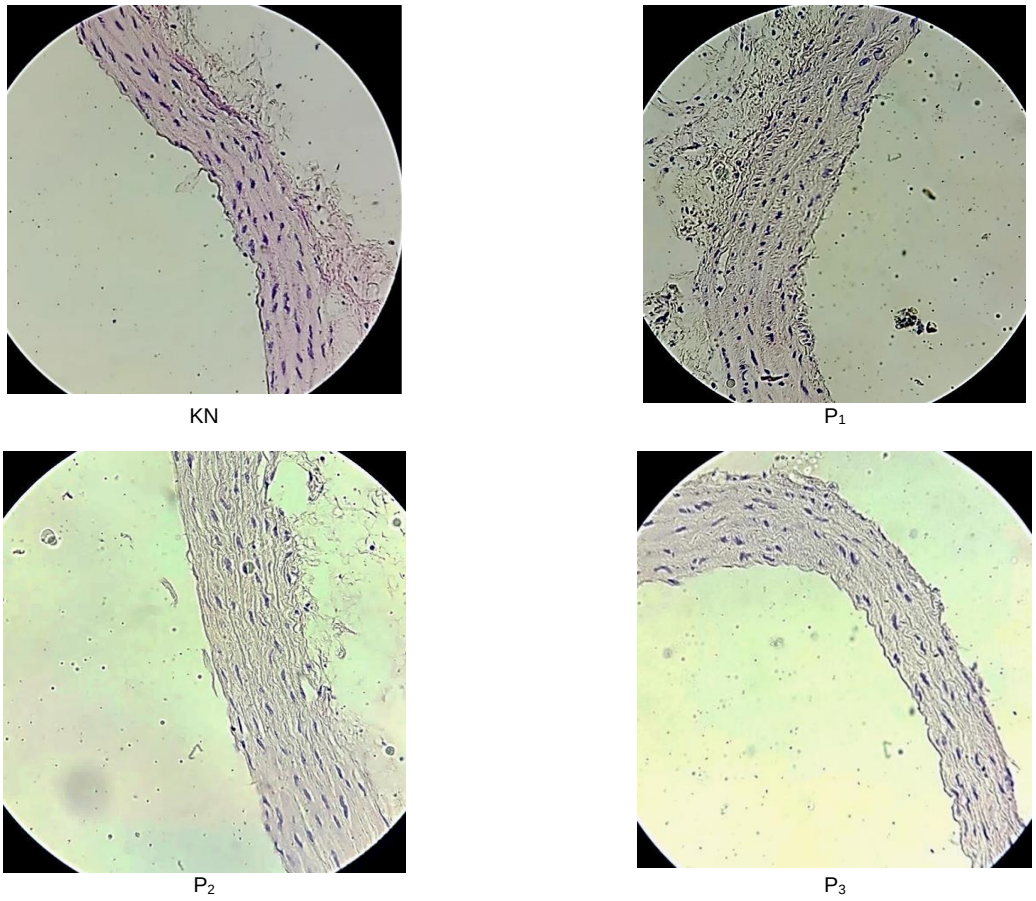

Figure 2. Foam cells in the heart aorta of each group (100x magnification)

Foam cells are formed by consuming foods containing saturated fatty acids, such as duck egg yolks, quail egg yolks, and hardened (trans) used cooking oil, which can worsen cholesterol levels. Trans fats can cause an increase in *low density lipoprotein* (LDL) and a decrease in *high density lipoprotein* (HDL). Hypercholesterolemia can interfere with endothelial performance by increasing the production of oxygen free radicals. Free radicals will inactivate nitric oxide, which is *the main endothelial relaxing* factor. Lipoproteins will accumulate in the tunica intima layer at the site of increased endothelial permeability. Exposure to free radicals in the endothelial cells of the artery wall will cause LDL oxidation. LDL oxidation can be captured by macrophages through *scavenger* receptors, if exposed to oxidized LDL, macrophages will form foam cells (Pabane, 2014).

Phytochemical testing was conducted to check the content of secondary metabolite compounds in binahong leaf extract. Tests include alkaloids, flavonoids, saponins, tannins, steroids/triterpenes, and glycosides. The test results were positive for alkaloids, flavonoids, saponins, tannins, and steroids/triterpenes positive. However, the glycoside test was not positive.

The results of the One-Way Anova test showed a significance value of 0.000 or less than 0.05, indicating a significant difference between the control and treatment groups. The analysis of the Post Hoc LSD test in this study showed a significance value of 0.000 or less than 0.05, which means that the group was significantly different from other groups.

The results of the analysis showed a significant difference between the control group and treatment group 1 (p = 0.000) and treatment group 2 (p = 0.000). Meanwhile, the control and treatment groups 3 had no significant difference (p = 0.849).

Histopathological observations were performed using a light microscope with a 400x magnification. The purpose of this observation is to see the structure and morphology of cells, especially fibroblast cells, in each heart function in the treatment group with the administration of binahong leaf extract with a dose of 200 mb/bb, a dose of 300 mb/BB and finally a dose of 400 mb/BB. The results of histopathologic examination of cardiac function in white rats fed high-fat feed and binahong leaf extract in the treatment period showed differences in the number and density of fibroblasts.

Table 4. One Way Anova *Test Results* on Urea Levels

	Sum	df	Mean square	F	Sig
Between Groups	4806.404	3	961.281	387.134	.000
In Groups	46.936	20	3.163		
Total	4863.34	23			

Table 5. Post-Hoc LSD Test Results on ALT Levels

Groups		Mean difference	Sig
Control	Treatment 1	1.80000*	.000
	Treatment 2	4.23333*	.000
	Treatment 3	8.11667*	.000
P1	Control	-1.95000*	.000
	Treatment 2	3.63333*	.000
	Treatment 3	7.61667*	.000
P2	Control	-.4.53333*	.000
	Treatment 1	-2.63333*	.000
	Treatment 3	6.96667*	.000
P3	Control	-8.51667*	.000
	Treatment 1	-6.61667*	.000
	Treatment 2	-3.73333*	.000

The number of fibroblast cells in the control group given pellet feed without binahong leaf extract was less and rare. Treatment Group 1 by giving pellet feed and administering binahong leaf extract at a dose of 200 mg/BB showed increased fibroblasts. The Treatment 2 group, fed pellets and given binahong leaf extract at a dose of 300 mg/BB, showed increased fibroblast cells and closer together. The Treatment 3 group, given pellet feed and administered binahong leaf extract at a 400 mg/BB dose, showed a more significant amount and density than the other groups. Based on histopathological observations, the group fed with pellets of binahong leaf extract at a dose of 400 mg/BB showed the presence of fibroblasts that were the most abundant and dense compared to other groups.

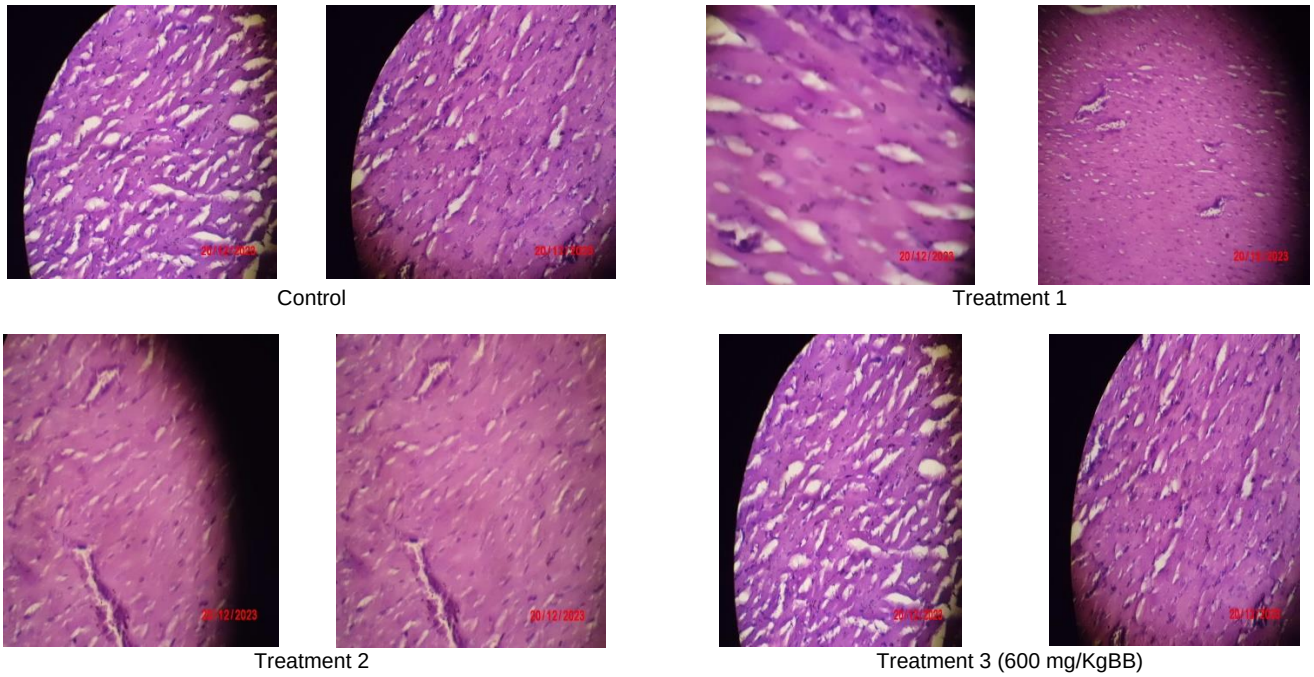

Figure 3. Histopathological Features of the Heart

Discussion

This study investigated the effects of binahong leaf extract (Anredera cordifolia) on cardiac function in male Wistar rats (Rattus norvegicus) fed a high-fat diet. A total of 24 Wistar rats were used, divided into four groups. Post-treatment observations revealed that the control group (K) had an average body weight of 235.50 g, while the treatment groups (P1, P2, P3) had weights of 275.75 g, 254.00 g, and 268.25 g, respectively. Body weights in the treatment groups decreased after administering the binahong extract, while the control group increased.

The administration of a high-fat diet (3 mL/200 g BW) for 14 days increased body weight in groups P1, P2, and P3. The differences in weight gain could be attributed to individual physiological responses, stress during handling, blood sampling, weighing, or cleaning cages (Wulan, 2014). Widyaningsih (2015) found no significant weight gain differences among groups after a high-fat diet, likely due to stress and excess physical activity. After administering binahong extract at 200 mg/kg BW, 300 mg/kg BW, and 400 mg/kg BW for two weeks, weight gain was observed in treatment groups P1, P2, and P3, while the control group experienced weight loss. This suggests that the extract did not significantly reduce body weight. Obesity is associated with higher blood pressure due to fat plaque accumulation in blood vessels, forcing the heart to pump blood harder. However, elevated blood pressure can also occur in individuals with normal weight due to age, diet, and physical inactivity.

The administration of binahong leaf extract at doses of 200 mg/kg BW, 300 mg/kg BW, and 400 mg/kg BW for two weeks had varying effects on body weight. In the treatment groups (P1, P2, P3), an increase in body weight was observed, while the control group experienced a decrease in weight. This indicates that the administered doses of binahong leaf extract did not significantly contribute to weight loss in the rats. Similarly, no significant weight gain was recorded in the control group, which was fed a high-fat diet. Research indicates that obesity is associated with higher blood pressure than normal weight. Weight gain correlates with plaque (fat) accumulation in the body, causing the heart to work harder to pump blood due to narrowed blood vessels. However, increased blood pressure can also occur in individuals with normal weight, influenced by factors such as age, diet, and physical inactivity

The administration of binahong leaf extract at 200 mg/kg BW, 300 mg/kg BW, and 400 mg/kg BW for two weeks showed varying effects on body weight. The treatment groups (P1, P2, P3) experienced weight gain, while the control group had a decrease in weight. This suggests that the binahong leaf extract did not significantly contribute to weight loss, and the high-fat diet in the control group did not result in significant weight gain. The animals underwent a pre-conditioning phase with a high-fat diet of quail egg yolks for 14 days before treatment. They were then divided into four groups: a control group receiving distilled water, and treatment groups receiving binahong leaf extract at 200 mg/kg BW (P1), 300 mg/kg BW (P2), and 400 mg/kg BW (P3). The study evaluated the extract's effectiveness in reducing cholesterol levels and improving cardiac function in hypercholesterolemic Wistar rats, identifying the 400 mg/kg BW concentration as the most effective. The findings highlight the potential of binahong leaf extract in managing hypercholesterolemia and associated cardiac dysfunctions.

The study was conducted over a 14-day observation period, generating data that required processing and testing. Initial data processing involved normality testing using the Kolmogorov-Smirnov test in SPSS. The results showed a significance value of 0.000 for all groups, indicating that the data were normally distributed and representative of the population. The normally distributed data were further tested for homogeneity using Levene’s test to determine whether the groups shared equal variances. The results showed significance values of 0.976 for aortic wall thickness and 2.057 for foam cell count, more significant than 0.05. This confirmed that the control and treatment groups (P1, P2, P3) were homogeneous and originated from the same population.

The homogeneous and normally distributed data were analyzed for effectiveness and significance using a One-Way ANOVA test, which yielded a significance value of 0.000 ($p < 0.05$). This indicated significant differences among the control and treatment groups, necessitating further analysis using a Post-Hoc LSD test. The Post-Hoc LSD analysis revealed a significance value of 0.000 ($p < 0.05$) for all groups, confirming that each group significantly differed from the others in terms of LDL cholesterol levels. The findings showed that the binahong leaf extract with a dose of 400 mg/kg BW (P3) substantially reduced

aortic wall thickness. In contrast, the 200 mg/kg BW (P1) and 300 mg/kg BW (P2) doses had less impact. The extract's efficacy is attributed to the antioxidant properties of flavonoids in binahong leaves, which scavenge free radicals and enhance endothelial function. Foam cell formation, a marker of atherosclerosis, is influenced by the consumption of saturated fats such as quail egg yolks, duck egg yolks, and hardened trans fats, which can increase low-density lipoprotein (LDL) levels and decrease high-density lipoprotein (HDL) levels. Hypercholesterolemia disrupts endothelial function by increasing reactive oxygen species (ROS), which deactivate nitric oxide, the primary endothelial relaxing factor. LDL accumulates in the tunica intima of blood vessels where endothelial permeability is increased. Exposure of endothelial cells to ROS causes LDL oxidation. Oxidized LDL is captured by macrophages through scavenger receptors, leading to the formation of foam cells. The binahong extract’s antioxidant properties mitigate these effects by reducing oxidative stress and improving vascular health.

Conclusion

Binahong leaf extract effectively improves the histopathological condition of the aorta in hypercholesterolemic Wistar rats, primarily due to its flavonoid content. Flavonoids are potent antioxidants that reduce aortic wall thickness and foam cell formation by scavenging free radicals and improving endothelial function.The most significant effect on aortic wall thickness was observed in the treatment group P3, which received a 400 mg/kg BW dose of the extract. In contrast, treatment groups P1 (200 mg/kg BW) and P2 (300 mg/kg BW) showed less impact. This highlights the dose-dependent efficacy of binahong extract in vascular repair. P3 (400 mg/kg BW) was the most effective in reducing foam cell formation. The flavonoids in binahong play a crucial role in lowering cholesterol, triglycerides, and LDL levels while increasing HDL levels. They also inhibit foam cell formation, preventing early atherosclerotic lesion development. These findings confirm the potential of binahong extract as a therapeutic agent for managing hypercholesterolemia and its associated vascular complications.

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