JMU
Jurnal Medika Udayana

ISSN: 2597-8012 JURNAL MEDIKA UDAYANA, VOL. 15 NO.7, JULI, 2026

Received: 2026-01-07 Revision: 2026-04-13 Accepted: 30-06-2026

ADMINISTRATION OF SACHA INCHI (*PLUKENETIA VOLUBILIS*) OIL CAUSES THINNER LEFT VENTRICULAR MYOCARDIUM IN MALE WISTAR RATS (*RATTUS NORVEGICUS*) GIVEN A HIGH-FAT AND HIGH-FRUCTOSE DIET

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ABSTRACT

Background: High-fat and high-fructose diet (HFHFD) is a major risk factor for obesity. Obesity causes adipocyte dysfunction, pro-inflammatory cytokines release, and insulin resistance. This leads to oxidative stress and impaired glucose metabolism, triggering cardiac remodelling (left ventricular hypertrophy). Sacha inchi oil (*Plukenetia volubilis*) is high in omega-3, omega-6, omega-9, and antioxidants, which can reduce left ventricular myocardial thickness. This study aimed to determine the effect of HFHFD and sacha inchi oil on left ventricular myocardial thickness.
Methods: This study used an experimental design, post-test only control group, with 25 heart samples of Wistar rats, randomly divided into 5 groups (n=5). There were groups given a normal diet (KN0), HFHFD (KN-), and HFHFD with sacha inchi oil at doses of: 0.27 ml/200 g BW (KP1), 0.54 ml/200 g BW (KP2), and 1.08 ml/200 g BW (KP3).
Results and discussion: Administration of HFHFD significantly thickened left ventricular myocardium of KN- ($p=0.01$) compared to normal diet (KN0) with an average thickness of 2980.05 ± 216.07 µm and 2443.17 ± 215.07 µm. Administration of sacha inchi oil (KP1, KP2, and KP3) significantly thinned left ventricular myocardium ($p<0.01$) compared to negative control group (KN-) with an average myocardial thickness of 2237.14 ± 222.29 µm; 1955.27 ± 317.35 µm; 1709.80 ± 137.16 µm and 2980.05 ± 216.07 µm.
Conclusion Based on the results, DTLF causes left ventricular myocardial thickening and administration of sacha inchi (*Plukenetia volubilis*) oil causes left ventricular myocardial thinning. Therefore, administration of sacha inchi (*Plukenetia volubilis*) oil has the potential to prevent myocardial thickening.

Keywords : High-fat and high-fructose diet, Cardiomyopathy, Sacha Inchi Oil

INTRODUCTION

The prevalence of cardiometabolic syndrome, dyslipidemia, and obesity in Indonesia is 21.66%, 20% (aged 12-19 years), and 33% (adults), respectively.[1,2] Cardiometabolic syndrome encompasses the conditions of obese cardiomyopathy, insulin resistance, dyslipidemia, and hypertension. A high-fat and high-fructose diet (HFHFD) is a major risk factor for cardiometabolic syndrome. Therefore, we can conclude that cardiometabolic syndrome, dyslipidemia, and obesity are major interrelated risk factors for cardiovascular disease (including obese cardiomyopathy), caused by chronic consumption of HFHFD.[3,4]

Dyslipidemia is an imbalance in the lipid profile, characterized by increased triglycerides (serum TG ≥150 mg/dl), increased low-density lipoprotein (LDL ≥140 mg/dl), and decreased high-density lipoprotein (HDL <35 mg/dl for men and <40 mg/dl for women by WHO).[5] HFHFD diet can cause dyslipidemia by promoting excessive lipogenesis from fructose and damaging the lipid profile (increasing LDL and TG and decreasing HDL) due to its high fat content. In dyslipidemia, the lipid profile is atherogenic, thus increasing the risk of cardiovascular disease. In this condition, abnormal fatty acid metabolism occur and apolipoprotein B (ApoB) is high. This causes inflammation of the tunica intima of blood vessels. Furthermore, LDL infiltration occurs, which adds to the damage by exacerbating the inflammatory reaction, oxidation, and macrophage infiltration, ultimately leading to atherosclerosis. Atherosclerosis causes myocardial infarction and accelerates cardiac aging and remodeling.[6–8]

Obesity is defined by the World Health Organization (WHO) as a pathological condition characterized by abnormal (excessive) fat accumulation. Adipose tissue has endocrine and immune regulatory functions.[8] A HFHFD diet results in adipocyte dysfunction (obesity) with chronic excess energy accumulation.

This excess energy is stored in fat, transforming adipocytes from a lean state to an obese state (adipocyte dysfunction). In obese state, adipocytes are exposed to chronic excess energy. This triggers proinflammatory immune cell infiltration through the release of proinflammatory factors by adipocytes and a decrease in anti-inflammatory adipokines. These released proinflammatory factors are called adipocytokines (adiponectin, resistin, leptin, IL-6, IL-1β, tumor necrosis factor-α (TNF-α), and other proinflammatory cytokines). Chronic inflammation leads to the production of reactive oxygen species (ROS). Without antioxidant to balance the ROS, oxidative stress will occur.[8,9] Oxidative stress impacts the structure and function of the heart (cardiomyopathy). Other than that, Chronic inflammatory conditions cause lipotoxicity in non-fat tissues such as the liver and muscle, thereby impairing insulin sensitivity (insulin resistance).[6–8,10] Insulin resistance will also disrupt glucose metabolism as energy for heart function, thereby worsening the cardiac remodeling process in the heart. This condition is termed as obesity cardiomyopathy.[7]

Obesity cardiomyopathy manifests as left ventricular (LV) enlargement that can lead to heart failure and is a disorder resulting from cardiometabolic syndrome and obesity.[6,7,11] Obesity cardiomyopathy increases the risk of heart failure, generally in the form of coronary heart disease (CHD), which is the number one cause of death worldwide (17.9 million deaths per year).[12] Therefore, cardiometabolic syndrome, dyslipidemia, and obesity increase the risk of heart failure by causing obesity cardiomyopathy.[8]

One indicator used to detect structural abnormalities in the heart is measuring myocyte thickness. In obese cardiomyopathy, there is concentric thickening of the heart muscle layer. Concentric thickening of the heart muscle (hypertrophy) is associated with decreased heart function and is a cause of heart failure.[13–15]

Herbal remedies for non-communicable diseases are being widely developed, including sacha inchi oil (Plukenetia volubilis). Sacha inchi oil contains high levels of omega-3, omega-6, omega-9, and antioxidants. Each of these compounds contributes to the prevention of obese cardiomyopathy in its own way and acts synergistically with one another. Sacha inchi oil can balance lipid profiles, have anti-inflammatory effects, act as a radical scavenger, and enhance the effects of endogenous antioxidants.[16–19] Therefore, consuming sacha inchi oil can prevent obese cardiomyopathy.

This study aimed to determine the effect of HFHFD and sacha inchi oil on left ventricular myocardial thickness. Through this research, we hope to contribute to a better understanding of the effect of HFHFD and sacha inchi oil towards myocardial structure (thickness) and provide preliminary data that may serve as a foundation for future research in this field.

MATERIALS AND METHODS

This is an experimental research with randomized post-test only control group design. This research is in vivo, using rats as subject. This study has received ethical feasibility by the Research Ethics Commission Unit, Faculty of Medicine, Udayana University, No. 2368/UN14.2.2.VII.14/LT/2025. The experimental animals were randomly allocated into five experimental groups with following characteristics: Adult male Wistar rats (3-4 months old) that weighed between 180-260 grams. The rats were treated and cared for in the Integrated Biomedical Laboratory, Faculty of Medicine, Udayana University. Preparation and examination of histological slides were conducted at the histology laboratory, Faculty of Medicine, Udayana University.

ANIMAL MAINTENANCE

The rats are acclimatized for 7 days and maintained under controlled environmental conditions (28°C and 50% humidity). The rats were placed in a 12-hour period without light in the morning, while the following 12 hours (at night) were illuminated with 10-watt lamp. If a rat was found to be sick, consultation to veterinarian is done immediately. During acclimatization, rats were given standard feed brand 594 (contains 17.5-19.5% protein, 40-50% carbohydrate, 3% fat, 8% fiber, 0.9% calcium and 0.6% phosphorus), which was given ad libitum at 20g/ day. Drinks were also given ad libitum.

ALLOCATION OF SAMPLE GROUPS

This study uses five groups. It was determined that the number of samples needed for each group was 5 animals based on Federer's formula with the consideration of 10% mortality of experimental animals. The groups were divided as follows:

a. Normal control (KN0): Normal control group was given standard food for 28 days
b. Negative control (KN-): Negative control group was given high fat and fructose diet (HFHFD) and distilled water for 28 days.
c. Treatment 1 (KP1): The treatment group 1 was given HFHFD and sacha inchi oil at a dose of 0.27 ml/200 g BB/day for 28 days.
d. Treatment 2 (KP2): The treatment group 1 was given HFHFD and sacha inchi oil at a dose of 0.54 ml/200 g BB/day for 28 days.
e. Treatment 3 (KP3): The treatment group 1 was given HFHFD and sacha inchi oil at a dose of 1.08 ml/200 g BB/day for 28 days.

TREATMENT

After the adaptation period, on day 8, the normal control group (KN0) was given a normal diet, the negative control group (KN-) was given HFHFD, and the treatment group (KP1, KP2, KP3) was given HFHFD and sacha inchi oil (SIO) at the following doses: 0.27 ml/200 g body weight per day, 0.54 ml/200 g body weight per day, and 1.08 ml/200 g body weight per day. The mice were weighed weekly to adjust the dosage to their body weight in anticipation of any weight gain during treatment. The

remaining feed was weighed daily to determine the amount of food left over.

The high-fat diet was a combination of 85% standard feed, 15% lard, and duck egg yolk. The standard feed was brand 594. The lard was heated until melted and administered at a rate of 3 ml per duck egg per day, mixed with the feed. Duck eggs were cooked and the yolk was removed, administered at a rate of 2 ml per duck egg per day by tube once daily at 4:00 PM. A standard diet of 20 grams per rat per day was provided in the morning. Drinking water mixed with 30% fructose was provided ad libitum (100 ml of 55% fructose + 80 cc of distilled water = 180 ml of 30% fructose).

The sacha inchi oil used was a product under the brand name "Sacha Inchi Oil," produced by House of Sachi, Cikarang, West Java, with registration number P-RIT 8063216010289-27. The rats were administered orally via a tube once daily at 8:00 a.m., at doses of 0.27 ml per 200 g of body weight per day, 0.54 ml per 200 g of body weight per day, and 1.08 ml per day for 28 days. An eight-hour interval between the administration of the sacha inchi oil and the high-fat diet was provided.

EUTHANIZATION OF THE SAMPLE

On the 29th day, euthanasia was performed using 10% ketamine HCL at a dose of 0.2 ml/200 g of mouse body weight. The heart was collected and stored in formalin before being paraffinized. The mice were then burned in accordance with ethical procedures.

HEMATOXYLIN EOSIN STAINING

The organs (hearts) were prepared in paraffin blocks, sliced with a microtome at a thickness of 4 µm to allow transverse viewing of the heart. The sliced tissue underwent deparaffinization with xylene I and II solutions for 5 minutes each. The slides are the dehydrated in ethanol I and II for 5 minutes each, then rinsed with water for 1 minute. After dehydrated, the slides were stained with hematoxylin for approximately 15 minutes and were rinsed with water to stain the cell nuclei. The slides were then stained with eosin for approximately 4 minutes and rinsed with water to stain the cytoplasm. The slides were rehydrated by immersing them in 70%, 80%, and 96% alcohol for 3 minutes each. The slides were then immersed in xylene for 3 minutes. The slides were dried and were applied an adhesive, then covered by coverslip.

HISTOLOGICAL PBSERVATIONS

The histological slides of the heart were observed using a binocular microscope (Olympus CX21) with 12.5x magnification in 5 fields of view (apical, mid-lateral, basal lateral, septal, and basal septal) on each sample preparation connected to an Optilab® camera. In each field of view, left ventricular myocardial thickness was measured 5 times, then averaged using Image Raster® software. The results from the 5 fields of view were then averaged again to obtain the myocardial thickness in each sample.

After the adaptation period, on day 8, the normal control group (KN0) was given a normal diet, the negative control group (KN-) was given HFHFD, and the treatment group (KP1, KP2, KP3) was given HFHFD and sacha inchi oil (SIO) at the following doses: 0.27 ml/200 g body weight per day, 0.54 ml/200 g body weight per day, and 1.08 ml/200 g body weight per day. The mice were weighed weekly to adjust the dosage to their body weight in anticipation of any weight gain during treatment. The remaining feed was weighed daily to determine the amount of food left over

HISTOLOGICAL OBSERVATION

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DATA ANALYSIS

The average myocardial thickness of each sample is presented in micrometer (µm). The data is numerical (ratio). Using SPSS 26.0 software, descriptive and analytical statistical analysis was done to evaluate variations of myocardial thickness. Descriptive analysis that was done to the samples are: Mean, standard deviation, median, minimum, and maximum values of left ventricular myocardial thickness data. The data are presented in tables and graphs.

The analytical statistical tests used were a parametric one-way ANOVA test and a post-hoc analysis using the LSD test to determine differences between groups and determine the most likely cause of the thinnest left ventricular myocardial thickness. The parametric test was performed because the data were normal when tested using the Shapiro-Wilk test (small sample size). The LSD test was performed because the data distribution was homogeneous when tested using Levene's test.

RESULT

The samples were first analyzed descriptively. Figure 1 shows sample measurements in each group (apical view) and table 1 displays results of the average left ventricular myocardial thickness in each group.

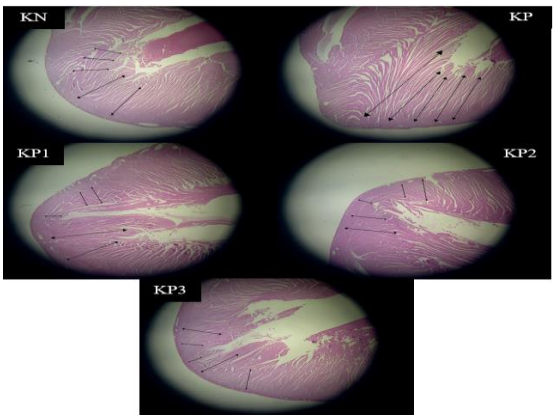

Figure 1. Apical histology image of the left ventricle of each group at 12.5x magnification

Based on figure 1, we can see a trend that if given HFHFD alone (KP), the myocardium thickened, but if given sacha inchi oil (KP1, KP2, KP3), the myocardium thinned as in KN (given nothing).

The results of the average left ventricular thickness in the five groups showed that the highest average left ventricular thickness in the sample was in the KN- group with an average of 2980.05 ± 216.07 µm and the lowest in the KP3 group with an average of 1709.80 ± 137.16 µm.

Table 1. Descriptive Analysis Results of Left Ventricular Myocardial Thickness after Administration of Sacha Inchi Oil (*Plukenetia volubilis*)

Group	Mean± S.D (µm)	Minimal	Maximal
KN0	2443,17 ± 215,07	2658,24	2228,10
KN-	2980,05 ± 216,07	3196,57	2764,43
KP1	2237,14 ± 222,29	2459,43	2014,85
KP2	1955,27 ± 317,35	2272,62	1637,92
KP3	1709.80 ± 137,16	1846,96	1572,64

S.D: Standard deviation.

The normality test used on a total of 25 samples was the Shapiro-Wilk Test. Result showed normal distribution (p value > 0.05) in all groups. Data homogeneity testing using the Levene Test obtained homogeneous data, with a p value > 0.05. The results of data normality and homogeneity can be seen in Table 2.

Table 2. Results of data normality and homogeneity of left ventricular myocardial thickness

Group	Normality Test	Homogeneity Test
KN0	p=0,311	
KN-	p=0,234	
KP1	p=0,290	p=0,105
KP2	p=0,299	
KP3	p=0,213	

The left ventricular myocardial thickness data were normally distributed and the data variance was homogeneous, therefore the hypothesis test was continued with a one-way ANOVA test with a post-hoc LSD Test. The results of the one-way ANOVA test of left ventricular myocardial thickness showed a value ($p<0.05$), which indicates a statistically significant difference in the average left ventricular myocardial thickness between groups (at least 1 pair), which can be seen in Table 3.

Table 3. Results of Analysis of Differences in Mean Left Ventricular Myocardial Thickness between Groups

Group	Number of Samples	(Mean ± S.D) µm	P value
KN0	5	2443,17 ± 215,07	
KN-	5	2980,05 ± 216,07	
KP1	5	2237,14 ± 222,29	0,01
KP2	5	1955,27 ± 317,35	
KP3	5	1709.80 ± 137,16	

S.D: Standard deviation.

Results of the one-way ANOVA test had a p-value <0.05, thus a post-hoc analysis was conducted to determine significant differences between groups. Two pairs of groups showed no significant differences, namely KN0 and KP1, and KP2 and KP3 (p>0.05). Sorting myocardial thickness from thickest to thinnest resulted in KN- > KN0 = KP1 > KP2 = KP3. The results of the post-hoc analysis can be seen in Table 4.

Table 4. Results of post-hoc LSD test of the mean left ventricular myocardial thickness between groups

Group	Mean Differences	*95%CI*		*P*
		Minimum	Maximum	
KN0 vs KN-	-536,87	-838,80	-234,95	0,001
KN0 vs KP1	206,03	-95,89	507,96	0,170
KN0 vs KP2	487,90	185,98	789,83	0,003
KN0 vs KP3	733,37	431,45	1035,29	<0,001
KN- vs KP1	742,91	440,99	1044,84	<0,001
KN- vs KP2	1024,77	722,85	1326,70	<0,001
KN- vs KP3	1270,24	968,32	1572,17	<0,001
KP1 vs KP2	281,86	-20,06	583,79	0,066
KP1 vs KP3	527,33	225,40	829,26	0,002
KP2 vs KP3	245,47	-56,46	547,39	0,105

DISCUSSION

Research findings support the hypothesis that a high-fat and fructose diet (HFHFD) results in a thicker left ventricular myocardium in male Wistar rats (*Rattus norvegicus*) compared to a normal diet. Post-hoc test results showed that the left ventricular myocardial thickness in the group fed a DTLF (KN-) was significantly thicker (p=0.001) than in the group fed a normal diet (KN0) (2980.05 ± 216.07 vs. 2443.17 ± 215.07 µm). This finding which is consistent with previous studies by Kang et al., 2015, showing that giving high fat diet significantly thickens the left ventricular posterior diastolic thickness (p<0.05). Therefore, Kang et al.'s study aligns with the authors' research.[20]

A high-fat and high-fructose diet is a risk factor for cardiometabolic syndrome, obesity, and dyslipidemia. This results in adipocyte dysfunction, resulting in increased adipocytokines, which cause systemic chronic inflammation and insulin resistance, which disrupts glucose metabolism.[8,21] Chronic inflammation and impaired glucose metabolism cause obese cardiomyopathy through the mechanism of excessive free radical generation, resulting in oxidative stress. In conditions of oxidative stress and excessive inflammation, cardiac remodeling occurs as a compensatory mechanism. Hemodynamic changes occur as a consequence of cardiac remodeling and also act as a factor that exacerbates remodeling. In obese cardiomyopathy, cardiac remodeling manifests as left ventricular enlargement (LVH). Therefore, the histological findings of this study are in line with existing theories.[6–8]

Research findings support the hypothesis that oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 0.27 ml/200 g BW causes the left ventricular myocardium to be thinner in the hearts of male Wistar rats (*Rattus norvegicus*) given a high-fat and fructose diet (HFHFD). Post-hoc test results showed that the left ventricular myocardial thickness in treatment group 1 (KP1) which was given HFHFD and sacha inchi oil at a dose of 0.27 ml/200 g BW was significantly thinner (p<0.001) compared to the treatment group (KN-) which was given HFHFD alone (2237.14 ± 222.29 vs 2980.05 ± 216.07 µm).

This finding is consistent with previous studies by Habicht et al., 2020, showing that docosahexaenoic acid in low dose (supplementation) reduces mRNA expression of TNF-alpha, IL-10 and improves ejection fraction (p<0.05). Sacha inchi oil contains high level of omega-3. Omega-3 is a precursor of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA); consequently it has similar benefits. Those findings indicate that docosahexaenoic acid (also implies for omega-3) reduces inflammation and improves heart function. Therefore, Habicht et al.'s study aligns with the authors' research.[22]

The high omega-3, omega-6, omega-9, and antioxidant content of sacha inchi oil contributes to the prevention of obesity cardiomyopathy, as measured by left ventricular myocardial thickness. The synergistic effect of omega-3, omega-6, omega-9, and antioxidants (tocopherols, flavonoids, and phenolics) can balance LDL and TG levels, and increase HDL. By balancing the lipid profile, sacha inchi oil can have anti-inflammatory and anti-radical effects (preventing oxidative stress).[23,24] The anti-inflammatory and anti-radical properties of sacha inchi oil can prevent cardiac remodeling, thereby minimizing the occurrence of left ventricular hypertrophy (cardiomyopathy).[17,25,26] At the appropriate dose, sacha inchi oil can achieve a synergistic effect in preventing obesity cardiomyopathy (cardioprotective) if the omega-6 to omega-3 ratio is ideal/low (1:1).[16,27] The omega-6 to omega-3 ratio in sacha inchi oil is 1:1.[28] Therefore, sacha inchi oil can reduce left ventricular thickness in rats given DTLF when administered at the appropriate dose.

The supplementation/low dose administered in this study is half the reference dose of sacha inchi oil for adult humans (70 kg). The reference dose of sacha inchi oil for adult humans is 30 ml/day, so the supplementation dose for adult humans is 15 ml/day.[29] When converted to a rat dose (200 g) with a conversion

factor of 0.018, the supplementation dose is 0.27 ml/200 g body weight/day.[28] Therefore, the administration of sacha inchi oil is in accordance with the supplementation dose, so sacha inchi oil can reduce left ventricular thickness and prevent cardiovascular disease.

Research findings support the hypothesis that oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 0.54 ml/200 g BW causes the left ventricular myocardium to be thinner in the hearts of male Wistar rats (*Rattus norvegicus*) given a high-fat and fructose diet (HFHFD). Post-hoc test results showed that the left ventricular myocardial thickness in treatment group 2 (KP2) which was given HFHFD and sacha inchi oil at a dose of 0.54 ml/200 g BW was significantly thinner ($p<0.001$) compared to the treatment group (KN-) which was given HFHFD alone (1955.27 ± 317.35 vs 2980.05 ± 216.07 µm).

This finding is consistent with previous studies by Ambulay et al., 2021, showing sacha inchi oil at a dose equivalent to the standard reference dose significantly reduces leptin, increases antioxidant recution activity, and increases the level of endogenous antioxidant (SOD) ($p<0.05$). Those findings indicate that sacha inchi oil significantly improves adipocytokines, improves antioxdiant activity, and has synergic effect towards endogenous antioxidant, which as a result give a cardioprotective effect. Therefore, Ambulay et al.'s study aligns with the authors' research.[30]

The standard dose administered in this study is the reference dose for sacha inchi oil administration in adult humans (70 kg). The reference dose for sacha inchi oil administration in adult humans is 30 ml/day.[29] When converted to a rat dose (200 g) with a conversion factor of 0.018, the standard reference dose is 0.54 ml/200 g body weight/day.[28] Therefore, the administration of sacha inchi oil meets the standard reference dose, suggesting that sacha inchi oil can reduce left ventricular thickness and prevent cardiovascular disease.

Research findings support the hypothesis that oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 1.08 ml/200 g BW causes the left ventricular myocardium to be thinner in the hearts of male Wistar rats (*Rattus norvegicus*) given a high-fat and fructose diet (HFHFD). Post-hoc test results showed that the left ventricular myocardial thickness in treatment group 3 (KP3) which was given HFHFD and sacha inchi oil at a dose of 1.08 ml/200 g BW was significantly thinner ($p<0.001$) compared to the treatment group (KN-) which was given HFHFD alone (1709.80 ± 137.16 vs 2980.05 ± 216.07 µm).

This finding is consistent with previous studies by Chrysohoou et al., 2016, included 205 patients with compensated chronic heart failure due to ischemic heart failure (IHF) or dilated cardiomyopathy (DCM) NYHA classification I-III under optimal medical care. Participants were randomly assigned 1 to 1 to receive 1000 mg omega-3-PUFA supplementation (high dose) or no supplementation, in a non-blinded manner. Echocardiographic assessments were performed at the first visit and 6 months later. The study showed that omega-3 at high dose significantly reduces BNP levels (p=0,001), reduces left ventricular end-diastolic (p=0,047) and end-systolic volume (p=0,001), reduces left atrial maximal diameter (p=0,004), and improves left atrial ejection fraction (p=0,021). Those findings indicate that omega-3 (which are abundant in sacha inchi oil) reduces risk of heart heart failure, improves heart function, and improves heart structure. A decrease in BNP levels indicates a decrease in heart failure biomarker levels (indicating improved heart health). Furthermore, a decrease in end-diastolic and end-systolic dimensions, a decrease in maximum diameter, and an improved ejection fraction indicate improved heart function and left ventricular structure (cardioprotective effect). Therefore, Chrysohoou et al.'s study aligns with the authors' research.[31]

The high dose administered in this study was twice the reference dose for sacha inchi oil in adult humans (70 kg). The reference dose for sacha inchi oil in adult humans is 30 ml/day, so the high dose for adult humans is 30 ml/day.[29] Converting this dose to a rat dose (200 g) with a conversion factor of 0.018 yields a supplemental dose of 1.08 ml/200 g body weight/day.[28] Therefore, the administration of sacha inchi oil is in accordance with the supplementation dose, so that sacha inchi oil can reduce the thickness of the left ventricle and prevent cardiovascular disease.

SUMMARY

Based on the research results, the administration of sacha inchi oil to rats fed a high-fat and fructose diet (HFHFD) for 28 days resulted in the following conclusions:

a. A high-fat and fructose diet (HFHFD) resulted in a thicker left myocardium in the hearts of male Wistar rats (*Rattus norvegicus*) compared to those on a normal diet.
b. Oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 0.27 ml/200 g body weight/day resulted in a thinner left ventricle in the hearts of male Wistar rats (*Rattus norvegicus*) fed a high-fat and fructose diet (HFHFD).
c. Oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 0.54 ml/200 g body weight/day resulted in a thinner left ventricle in the hearts of male Wistar rats (*Rattus norvegicus*) fed a high-fat and fructose diet (HFHFD).
d. Oral administration of sacha inchi oil (*Plukenetia volubilis*) at a dose of 1.08 ml/200 g BW/day caused a thinner left ventricle in the hearts of male Wistar white rats (*Rattus norvegicus*) given a high fat and fructose diet (HFHFD).

SUGGESTION

Based on the results and findings obtained in this study, the authors recommend:

a. Further research is needed regarding the toxicity test of long-term administration of sacha inchi (*Plukenetia volubilis*) oil in a high-fat and fructose diet (HFHFD).
b. Further research is needed regarding left ventricular myocardial measurements using stereohistology methods in the administration of sacha inchi (*Plukenetia volubilis*) oil in a high-fat and fructose diet (HFHFD).
c. Further research is needed on left ventricular function in the administration of sacha inchi (*Plukenetia volubilis*) oil in a high-fat and fructose diet (HFHFD).

ACKNOWLEDGEMENT

The authors would like to thank Doctor Debby Chesilya Wijaya who helped with this research by providing materials and treating the research samples.

REFERENCES

1. Herningtyas EH, Ng TS. *Prevalence and distribution of metabolic syndrome and its components among provinces and ethnic groups in Indonesia*. BMC Public Health 2019;19:377. https://doi.org/10.1186/s12889-019-6711-7.
2. Khan AR, Salama AH, Aleem Z, Alfakeer H, Alnemr L, Shareef AMM. *The Promising Frontier of Cardiometabolic Syndrome: A New Paradigm in Cardiology*. Cureus 2023;15:1–7. https://doi.org/10.7759/cureus.45542.
3. Abera A, Worede A, Hirigo AT, Alemayehu R, Ambachew S. *Dyslipidemia and associated factors among adult cardiac patients: a hospital-based comparative cross-sectional study*. Eur J Med Res 2024;29:237. https://doi.org/10.1186/s40001-024-01802-x.
4. Bays HE, Kirkpatrick C, Maki KC, Toth PP, Morgan RT, Tondt J, Christensen SM, Dixon D, Jacobson TA. *Obesity, dyslipidemia, and cardiovascular disease: A joint expert review from the Obesity Medicine Association and the National Lipid Association 2024*. Obes Pillars 2024;10:100108. https://doi.org/https://doi.org/10.1016/j.obpill.2024.100108.
5. Nwankwo M, Okamkpa CJ, Danborno B. *Comparison of diagnostic criteria and prevalence of metabolic syndrome using WHO, NCEP-ATP III, IDF and harmonized criteria: A case study from urban southeast Nigeria*. Diabetes Metab Syndr Clin Res Rev 2022;16:102665. https://doi.org/https://doi.org/10.1016/j.dsx.2022.102665.
6. Chrysohoou C, Fragoulis C, Leontsinis I, Gastouniotis I, Fragouli D, Georgopoulos M, Mantzouranis E, Noutsou M, Tsioufis KP. *Cardiometabolic Care: Assessing Patients with Diabetes Mellitus with No Overt Cardiovascular Disease in the Light of Heart Failure Development Risk*. Nutrients 2023;15. https://doi.org/10.3390/nu15061384.
7. von Bibra H, Paulus W, St. John Sutton M. *Cardiometabolic Syndrome and Increased Risk of Heart Failure*. Curr Heart Fail Rep 2016;13:219–29. https://doi.org/10.1007/s11897-016-0298-4.
8. Ren J, Wu NN, Wang S, Sowers JR, Zhang Y. *Obesity cardiomyopathy: Evidence, mechanisms, and therapeutic implications*. Physiol Rev 2021;101:1745–807.https://doi.org/10.1152/physrev.00030.2020.
9. Wu H, Ballantyne CM. *Metabolic Inflammation and Insulin Resistance in Obesity*. Circ Res 2020;126:1549–64. https://doi.org/10.1161/CIRCRESAHA.119.315896.
10. Feijóo-Bandín S, Aragón-Herrera A, Morańa-Fernández S, Anido-Varela L, Tarazón E, Roselló-Lletí E, Portolés M, Moscoso I, Gualillo O, González-Juanatey JR, Lago F. *Adipokines and inflammation: Focus on cardiovascular diseases*. Int J Mol Sci 2020;21:1–34. https://doi.org/10.3390/ijms21207711.
11. Bartkowiak J, Spitzer E, Kurmann R, Zürcher F, Krähenmann P, Garcia-Ruiz V, Mercado J, Ryffel C, Losdat S, Llerena N, Torres P, Lanz J, Stocker M, Ren B, Glöckler M, Pilgrim T. *The impact of obesity on left ventricular hypertrophy and diastolic dysfunction in children and adolescents*. Sci Rep 2021;11:13022. https://doi.org/10.1038/s41598-021-92463-x.
12. Ziegler T, Rahman FA, Jurisch V, Kupatt C. *Atherosclerosis and the capillary network; Pathophysiology and potential therapeutic strategies*. Cells 2020;9:1–13. https://doi.org/10.3390/cells9010050.
13. Armandi A, Rosso C, Caviglia GP, Bugianesi E. *Insulin Resistance across the Spectrum of Nonalcoholic Fatty Liver Disease*. Metabolites 2021;11. https://doi.org/10.3390/metabo11030155.
14. Engin AB. Mechanism of Obesity-Related Lipotoxicity and Clinical Perspective. In: ENGIN AB, ENGIN A, editors. Obes. Lipotoxicity, Cham: Springer International Publishing; 2024, p. 131–66. https://doi.org/10.1007/978-3-031-63657-8_5.
15. Wang X, Xu Z, Chang R, Zeng C, Zhao Y. *High-Fructose Diet Induces Cardiac Dysfunction via Macrophage Recruitment in Adult Mice*. J Cardiovasc Pharmacol Ther 2023;28:10742484231162248. https://doi.org/10.1177/10742484231162249.
16. Goyal A, Tanwar B, Kumar Sihag M, Sharma V. *Sacha inchi (Plukenetia volubilis L.): An emerging source of nutrients, omega-3 fatty acid and phytochemicals*. Food Chem 2022;373:131459. https://doi.org/10.1016/j.foodchem.2021.131459.
17. Oppedisano F, Macrì R, Gliozzi M, Musolino V, Carresi C, Maiuolo J, Bosco F, Nucera S, Zito MC, Guarnieri L, Scarano F, Nicita C, Coppoletta AR, Ruga S, Scicchitano M, Mollace R, Palma E, Mollace V. *The anti-inflammatory and antioxidant properties of n-3 PUFAs: Their role in cardiovascular protection*. Biomedicines 2020;8.

https://doi.org/10.3390/biomedicines8090306.

18. Bertoni C, Abodi M, D'Oria V, Milani GP, Agostoni C, Mazzocchi A. *Alpha-Linolenic Acid and Cardiovascular Events: A Narrative Review.* Int J Mol Sci 2023;24.https://doi.org/10.3390/ijms241814319.
19. Costa TJ, Barros PR, Arce C, Santos JD, da Silva-Neto J, Egea G, Dantas AP, Tostes RC, Jiménez-Altayó F. *The homeostatic role of hydrogen peroxide, superoxide anion and nitric oxide in the vasculature*. Free Radic Biol Med 2021;162:615–35.https://doi.org/10.1016/j.freeradbiomed.2020.11.021.
20. Kang KW, Kim OS, Chin JY, Kim WH, Park SH, Choi YJ, Shin JH, Jung KT, Lim DS, Lee SK. *Diastolic dysfunction induced by a high-fat diet is associated with mitochondrial abnormality and adenosine triphosphate levels in rats*. Endocrinol Metab 2015;30:557–68. https://doi.org/10.3803/EnM.2015.30.4.557.
21. Ramos-Arellano LE, Matia-Garcia I, Marino-Ortega LA, Castro-Alarcón N, Muñoz-Valle JF, Salgado-Goytia L, Salgado-Bernabé AB, Parra-Rojas I. *Obesity, dyslipidemia, and high blood pressure are associated with cardiovascular risk, determined using high-sensitivity C-reactive protein concentration, in young adults*. J Int Med Res 2020;48. https://doi.org/10.1177/0300060520980596.
22. Habicht I, Mohsen G, Eichhorn L, Frede S, Weisheit C, Hilbert T, Treede H, Güresir E, Dewald O, Duerr GD, Velten M. *DHA Supplementation Attenuates MI-Induced LV Matrix Remodeling and Dysfunction in Mice*. Oxid Med Cell Longev 2020;2020. https://doi.org/10.1155/2020/7606938.
23. Mariamenatu AH, Abdu EM. *Overconsumption of Omega-6 Polyunsaturated Fatty Acids (PUFAs) versus Deficiency of Omega-3 PUFAs in Modern-Day Diets: The Disturbing Factor for Their "Balanced Antagonistic Metabolic Functions" in the Human Body*. J Lipids 2021;2021:1–15. https://doi.org/10.1155/2021/8848161.
24. Nogoy KMC, Kim HJ, Lee Y, Zhang Y, Yu J, Lee DH, Li XZ, Smith SB, Seong HA, Choi SH. *High dietary oleic acid in olive oil-supplemented diet enhanced omega-3 fatty acid in blood plasma of rats*. Food Sci Nutr 2020. https://doi.org/10.1002/fsn3.1644.
25. Attia AA, Sorour JM, Mohamed NA, Mansour TT, Al-Eisa RA, El-Shenawy NS. *Biochemical, Histological, and Ultrastructural Studies of the Protective Role of Vitamin E on Cyclophosphamide-Induced Cardiotoxicity in Male Rats*. Biomedicines 2023;11. https://doi.org/10.3390/biomedicines11020390.
26. Pavithra K, Sathibabu Uddandrao V V., Chandrasekaran P, Brahmanaidu P, Sengottuvelu S, Vadivukkarasi S, Saravanan G. *Phenolic fraction extracted from Kedrostis foetidissima leaves ameliorated isoproterenol-induced cardiotoxicity in rats through restoration of cardiac antioxidant status*. J Food Biochem 2020;44:1–9. https://doi.org/10.1111/jfbc.13450.
27. Yanti S, Agrawal DC, Saputri DS, Lin HY, Chien WJ. *Nutritional Comparison of Sacha Inchi (Plukenetia volubilis) Residue with Edible Seeds and Nuts in Taiwan: A Chromatographic and Spectroscopic Study*. Int J Food Sci 2022;2022. https://doi.org/10.1155/2022/9825551.
28. Wijaya DC, Linawati NM, Dwipayana IMP, Winarti NW, Sugiritama W, Dwija IBNP. *Effects of Sacha Inchi (Plukenetia volubilis) Oil on Serum Interleukin 6 Levels and Foam Cell Count in Male Wistar Rats (Rattus norvegicus) Fed a High Fat and Fructose Diet*. Asian J Eng Soc Heal 2024;3:978–90. https://doi.org/10.46799/ajesh.v3i5.313.
29. Direktorat Pengawasan Keamanan, Mutu dan Ekspor Impor Obat N. *Badan Pengawas Obat dan Makanan Republik Indonesia*. Bpom Ri 2022:1–67.
30. Ambulay JP, Rojas PA, Timoteo OS, Barreto T V., Vila ZN, de los Santos MB, Eguiluz M, Colarossi A. *Oil emulsion from Plukenetia huayllabambana (Sacha inchi) modifies nitric oxide and leptin in the liver and antioxidant and inflammation markers in the adipose tissue in obese rats*. Funct Foods Heal Dis 2021;11:92–103. https://doi.org/10.31989/FFHD.V11I3.778.
31. Chrysohoou C, Metallinos G, Georgiopoulos G, Mendrinos D, Papanikolaou A, Magkas N, Pitsavos C, Vyssoulis G, Stefanadis C, Tousoulis D. *Short term omega-3 polyunsaturated fatty acid supplementation induces favorable changes in right ventricle function and diastolic filling pressure in patients with chronic heart failure; A randomized clinical trial*. Vascul Pharmacol 2016;79:43–50. https://doi.org/10.1016/j.vph.2016.01.005.