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Original Article

The Effect of Moringa Leaf Extract (Moringa Oliefera) On Triglyceride Levels in Streptozotocin Induced Type 2 Diabetes White Wistar Rats

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ABSTRACT

High blood sugar levels can hasten the liver's production of triglycerides. Normally, the body uses glucose as one of its energy sources. This study aimed to determine changes in the weight of mice and decrease triglyceride levels in mice by administering Moringa leaf extract. This type of research is a pure experiment with a "pre and post-randomized controlled group" design. This was carried out using a repeated ANOVA test, a sample of 25 mice. The research used male white rats of the Wistar strain, which were induced with STZ (Streptozotocin) at a dose of 65 mg/kg BW and NA 230 mg/kg BW, where the experimental animals were divided into 5 groups, namely negative control group, positive control and 3 treatment groups given the extract. from Moringa leaves at a dose of 200, 300, 400 mg/kg BW of rats. The optimal dose of Moringa leaves for losing weight and reducing triglyceride levels in mice is a dose of 400 mg/kg of mouse body weight. Glibenclamide (0.09 mg/kg rat body weight) and Moringa leaf extract (300 mg/kg rat body weight) are each the optimal dose to reduce glucose levels in rats. With a p value for each variable of 0.001, administration of Moringa leaf extract affected body weight, glucose and triglyceride levels in white Wistar rats with type 2 diabetes induced by streptozotocin. These findings suggest that Moringa leaf extract may have potential therapeutic effects in treating diabetes-related complications.

Keywords: *Rat Triglycerides, Blood Glucose, Moringa Leaf Extract, Streptozotocin*

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INTRODUCTION

The rapid progress of technology greatly affects people's quality of life. One of the bad impacts is the emergence of several degenerative diseases, such as diabetes mellitus[1,2,3]. This type of disease can be caused by a less active lifestyle and unhealthy eating habits. Apart from that, technological advances have also reduced people's physical activity levels, as evidenced by the increasing use of private transportation and the increasing use of computers in the workplace [4,5,6,7]. Additionally, the convenience and accessibility of modern technology has led to a sedentary lifestyle, where people spend more time engaging in screen-based activities than participating in physical exercise. Lack of physical activity not only contributes to the development of diseases such as diabetes mellitus but also increases the

risk of obesity and cardiovascular problems [8,9].

Excessive blood glucose levels can accelerate liver triglyceride production. One component of body fat is triglycerides. Triglycerides have normal functions in the body, such as as a source of energy, if levels are within normal limits [10]. However, high blood glucose levels can lead to higher triglyceride levels, which can result in a number of health problems. Obesity, heart disease, and diabetes are some of the diseases that high triglyceride levels can cause when triglyceride levels increase, this can contribute to the development of atherosclerosis, a condition characterized by the buildup of plaque in the arteries. This can increase the risk of heart attack and stroke [11,12]. Additionally, high triglyceride levels are often associated with insulin resistance, which is a key factor in the development of type 2 diabetes.

In the body, triglycerides and other fats are transported by unique molecules called lipoproteins. Because some lipoproteins with high triglyceride content also carry cholesterol, having high triglyceride levels can harm a person's health[13]. Those with high triglyceride levels are at risk of atherosclerosis, or narrowing of the artery walls. Fatty deposits that build up on artery walls cause atherosclerosis, which reduces blood flow and increases the risk of heart disease [14,15]. To stop the onset of atherosclerosis and its related problems, it is important to control triglyceride levels with a balanced diet, frequent exercise, and, if necessary, medication. Apart from diet and exercise, maintaining a healthy body weight is also important in controlling triglyceride levels. Excess weight can contribute to higher triglyceride levels and increase the risk of atherosclerosis. Monitoring triglyceride levels regularly and working with a healthcare professional can help individuals manage triglyceride levels effectively and reduce the risk of heart disease [11,16].

High triglyceride levels are associated with an increased risk of heart disease and other blood vessel disorders, such as low-density lipoprotein (LDL) cholesterol. People who have elevated triglyceride levels—the current upper limit is above 1.7 mmol/L—also often have elevated total, LDL, and HDL cholesterol levels. It resembles a trio. Although elevated triglyceride levels pose a potential danger, this is exacerbated if there is low HDL cholesterol, a situation commonly found in individuals with prediabetes or diabetes. The combination of high triglyceride levels with low HDL cholesterol can worsen the risk of heart disease and other blood vessel problems. People with diabetes or prediabetes are more likely to experience this combination, so it is important for them to control their lipid profile with lifestyle changes and medication if necessary [17].

Among the many uses of flavonoids are to protect cell structure, increase the effectiveness of vitamin C, reduce inflammation, stop bone loss, and act as an antibacterial [18]. The vitamin C present in powdered milk contributes to a healthy metabolism by increasing the amount of cholesterol produced in the form of fatty milk, increasing HDL cholesterol levels, and reducing the amount of powdered milk that is returned to the milk and converted into cholesterol [19].

This study aims to determine changes in the weight of mice and decrease triglyceride levels in mice by administering Moringa leaf extract. This research was carried out using experimental methods, where mice were divided into 5 groups, namely negative control group, positive control and three treatment groups which were given extract from Moringa leaves at doses of 200, 300, 400 mg/kg mice. The novelty of this research is that this study used Moringa leaf extract as an experimental material and observed changes in the mice's body weight and their triglyceride levels.

METHOD

Types and Research Design. The type of research used is a true experiment (pure experiment) using mice as test animals. The scope of scientific disciplines in this research includes the field of nutrition, it is pure experimental research in the field of nutrition using a pre and post randomized controlled group design approach. The study used male white Wistar rats induced by STZ (Streptozotocin) at a dose of 65 mg/kg BW and NA 230 mg/kg BW (Szkudelski, 2001), where the experimental animals were divided into 5 groups, namely: negative control group, positive control group and 3 Treatment groups were given extract from Moringa leaves at a

dose of 200, 300, 400 mg/kg BW of mice. The negative control group received a placebo, while the positive control group was administered a standard drug for comparison. The doses of Moringa leaf extract were chosen based on previous studies and their potential therapeutic effects on diabetes. Before being induced by STZ, the experimental animals were first checked for blood glucose levels and triglyceride levels to ensure that the experimental animals did not have diabetes or hypertriglyceridemia. Next, measurements of triglyceride levels in the blood of male white Wistar rats were carried out on the 5th day after induction. Mice were declared hypertriglyceridal if the triglyceride level in the blood was > 150 mg/dl (National Institute Health, 2001), then the negative control was only given distilled water, the positive control was given glibenclamide 0.09 mg/kg BW and the treatment group was given Moringa leaf extract to experimental mice at a dose of 200, 300 and 400 mg/kg BW of mice for 21 days. On days 9, 15 and 21, triglyceride levels in the blood were measured post test I II and III.

Dosage Calculation. Based on the research results of Setyawaty (2020 with the title Effectiveness of moringa oleifera on triglyceride levels in diabetic wistar rats (Rattus norvegicus) induced with streptozotocin (STZ), the minimum dose of administering Moringa leaf extract is 300mg/kg BW of rats)[20]. In this study, the dose given to mice with diabetes mellitus was 200mg, 300mg, 400mg of Moringa leaf extract. The dosage conversion rate for glibenclamide for humans with a body weight (BW) of 70 kg to mice with a BW of 200 g is 0.018. The therapeutic dose of glibenclamide in humans is 5 mg, then the dose for mice is 200 g, namely: 0.018 x 5 mg = 0.09 mg/ 200 g BW. Therefore, the dose of glibenclamide given to mice in this study was 0.09 mg/200 g BW.

Data Collection Procedure. The materials needed for this research are as follows. First, the test material is Moringa leaves (Moringan Oliefera) taken from the Jayapura City area. The ingredient for Moringa leaf extract is water. Second, white male Wistar rats aged 8 – 12 weeks, weighing 140 – 200 g and who meet the inclusion and exclusion criteria. Third, standard Comfeed feed given ad libitum to male white Wistar rats. Fourth, Streptozotocin (STZ) to induce experimental animals to develop diabetes mellitus at a dose of 65 mg/Kg BW. Fifth, the ingredients for measuring blood glucose levels are Glucose GOD FS Kit, phosphate buffer (Ph 7.5), Glucose Oxidase Phenol 4-Aminophenazone. Sixth, the ingredient for measuring triglyceride levels is Glycerol 3 phospar oxidase (GPO)

The tools used are first, tools for extracting Moringa leaves are mortar/blender, sieve, digital scale, measuring cup, 250 ml Erlenmeyer, 250 ml beaker glass, filter paper, glass funnel. Second, tools for keeping male white rats of the Wistar strain consist of digital scales, animal cages, standard feed containers and ad libitum drinking containers. Third, the tool for administering extracts from Moringa leaves is a gastric tube and the tool for induction of STZ and NA is a 3 ml sterile needle. Fourth, tools for measuring blood glucose levels consist of test tubes, micro pipettes, vortexes, glucose pipettes and spectrophotometers. Fifth, tools for measuring triglyceride levels consist of test tubes, micro pipettes, disposable syringes, centrifuges and spectrophotometers.

Making Moringa Leaf Powder. The ingredients used in making Moringa leaf extract are Moringa leaves, which are a type of tropical plant that is easy to grow in tropical areas like Indonesia. The water extraction method is as follows, Moringa leaves have been dried in the sun for 2-3 days until dry, some are left whole to dry and crushed. The powder is then extracted with water in a ratio of 1:10 (w/v), macerated at 500C for 3x24 hours, the extract obtained is filtered.

Preparation of Experimental Animals. In order to ensure the health aspects of experimental animals, maintenance of experimental mice is carried out at the Inter-University Research Center for Food and Nutrition Study Laboratory (PAU) Gadjah Mada University (UGM) Yogyakarta, taking into account the following matters. Firstly, mice are kept in individual cages that are ventilated and well lit, room temperature ranges from 28 – 320C. Second, food and drinks are provided ad libitum in the form of standard feed referring to the American Institute of Nutrition (AIN 93). Third, for health, the cage is cleaned every day. Fourth, the research began by preparing 25 white male Rattus norvegicus Wistar strain rats aged 8 – 12 weeks, which were adapted for 7 days with standard feeding. Fifth, the weight of the mice was weighed as basic data, then divided randomly into 5 groups, namely negative control, positive control and 3

treatment groups of 5 mice each. Sixth, the extract from Moringa leaves is given sonde, while normal feed and drink are given ad libitum.

Induction of Streptozotocin (STZ), Nicotinamide (NA) and Measurement of Blood Glucose and Triglyceride Levels in Experimental Rats. The induction of streptozotocin (STZ), nicotinamide (NA) and measurement of blood glucose and triglyceride levels in mice. The experiment was carried out in the first way. The mice that had been adapted for 1 week then had their blood taken to measure their initial glucose and triglyceride levels. Second, rats were then induced intraperitoneally with STZ at a dose of 65 mg/kg BW (100 mg STZ dissolved in 10 ml citrate buffer pH 4.5) and NA at a dose of 230 mg/kg BW (dissolved in 0.9% NaCl at a dose of 3 ml/ 200 g BB). NA induction was given 15 minutes before STZ induction in the 5 third treatment groups. Blood sampling for measuring blood glucose and triglyceride levels was carried out on the 5th day post-induction (pre test) to ensure that the mice really had diabetes mellitus. Before taking blood, the mice were fasted for 6 hours. Fourth, food and drink are still provided during treatment ad libitum. Fifth, blood sampling for measuring blood glucose and triglyceride levels was carried out on days 9, 15 and 21, as post-tests I, II and III. Sixth, blood glucose levels are measured quantitatively using the Enzymatic Colorimetric Test GOD – PAP method via the retro orbital plexus. Seventh, measurement of blood triglyceride levels is carried out quantitatively using the spectrophotometric method via the retro orbital plexus.

Extract from Moringa Leaves. Making Moringa leaf extract in the first way, powdered Moringa leaves are weighed according to the treatment, namely 200, 300 and 400 mg. secondly, the extract from Moringa leaves obtained was then filtered and then the extract from Moringa leaves was given to experimental mice in treatments III, IV and V. Sonde was given to mice for 21 days of treatment every morning.

Population and Sample. The population in this study was male white rats (Rattus norvegicus) of the Wistar strain. The samples in this study were male white Wistar rats aged 8 - 12 weeks, obtained from the Inter-University Research Center for Food and Nutrition Research Laboratory (PAU) Gadjah Mada University (UGM) Yogyakarta. The number of experimental animals used in this study was determined using the Faderer formula (Faderer, 1991), so that a sample of 4 mice was obtained.

The minimum number of experimental animals used is 4 animals. To avoid a shortage of experimental animals, 1 animal will be added to each treatment group so that 25 experimental animals are needed. The sampling technique for 20 mice was carried out by random sampling, divided into 5 groups. This random sampling technique ensures that each mouse has an equal chance of being selected for a treatment group. By adding one animal to each group, the researchers can ensure that there are enough animals to accurately represent the population and obtain reliable results.

The inclusion criteria in this study were first, male Wistar white rats aged 8 – 12 weeks with a body weight range of 140 – 200 g. Second, triglyceride levels in the blood > 150 mg/dL. Third, blood glucose levels ≥ 200 mg/dl after the fourth STZ induction. Rats are healthy, have no anatomical abnormalities and appear active. Meanwhile, the sample exclusion criteria were first, mice that looked sick (inactive movements), second, mice with extreme weight loss (>10%) before treatment. Third, mice died before and during treatment.

Before the analysis is carried out, the data that has been collected is checked for data completeness, coding, tabulated and entered into the computer. Data analysis includes descriptive and inferential statistical analysis. Descriptive analysis of data on changes in rat body weight, blood glucose levels and triglyceride levels expressed as mean and standard deviation. Data is presented in tabular form. The primary data in this study was data on changes in the mice's body weight, and changes in triglyceride levels between treatment groups were obtained from the results of laboratory examinations over 21 days. Laboratory data were analyzed statistically using the Repeated Anova test to determine the results of changes in the weight of mice and triglyceride levels in the blood of white mice. This analysis was tested using SPSS 16 software. Data from the analysis of rat body weight, changes in rat weight, and triglyceride levels in the experiment were presented in tabular form and narrated. Research reliability was assessed by calculating the Cronbach's alpha coefficient for the variables measured in the study. The results showed high internal

consistency, indicating that the data collected was reliable. Additionally, the researchers also conducted a post-hoc analysis to determine any significant differences between the treatment groups in terms of body weight and triglyceride levels.

The ethical test for this research, with number 003//KEPK/-J/XI/2019 from the Poltekkes kemenkes Jayapura, has been passed. Poltekkes Kemenkes Jayapura's ethical test makes sure the study complies with moral standards and protects participants' rights and welfare. This permission shows how dedicated the researchers are to carrying out their investigation in a morally and responsibly manner. By obtaining ethical approval, the researchers have demonstrated their commitment to upholding ethical principles and ensuring the well-being of the participants involved in the study. This approval also provides assurance that the research will be conducted with integrity and respect for all individuals involved.

RESULTS

The effect of giving Moringa leaf extract on rat weight and triglyceride levels in the blood on changes in rat weight. For changes in rat weight, the repeated ANOVA test was used to find out the difference between samples that took more than two measurements. Based on the results of measuring changes in rat weight using the repeated ANOVA test.

Table 1. Effect of giving Moringa leaf powder on changes in body weight in experimental mice.

BB Rat (gr)	Control Negative	Control Positive	Treatment I	Treatment II	Treatment III	p value
Initial Condition	175,60 (4,45)	171,20 (8,10)	180,20(11,96)	172,00 (12,39)	180,80(11,30)	
Pretreatment	180,80 (4,32)	174,60 (8,05)	184,20 (13,25)	175,40 (12,83)	184,40 (11,61)	
Initial DM	177,40 (5,03)	171,60 (8,50)	180,00(12,51)	172,40 (12,58)	180,40 (11,32)	
Day 9	174,20 (4,76)	177,00 (8,97)	184,20 (12,31)	177,20 (12,73)	185,60 (10,35)	0,001
Day 15	170,20 (4.55)	183,20 (8,64)	186,20 (13,14)	183,00 (11,81)	193,40 (11,54)	
Day 21	166,40 (4,77)	189,80(8,64)	190,60(15,24)	188,40(12,13)	199,00(10,97)	
Changes for 21 days	-14,4(0,45)	15,2 (0,41)	6,46(1,99)	13(-0,7)	14,6(-0,64)	

Based on Table 1. Using the Repeated ANOVA test, the results showed that there were differences in each treatment group with a value (Sig <0.05). In the table, the negative control was only given distilled water, the positive control was given glibenclamide 0.09 mg/200 g BW of mice, while treatments I, II and III were given extract from Moringa powder at doses of 200, 300 and 400 mg/kg BW of mice. So it can be said that there is an influence of giving Moringa leaf powder on changes in body weight of experimental mice. The most prominent changes in body weight were observed in mice given treatment III with an increase of 14.6 grams when compared to pre-treatment in the same group. The results of the study showed that there was a significant effect of administering Moringa leaf powder on changes in body weight in experimental mice. This can be seen from the most significant increase in body weight occurring in mice given treatment III with an increase reaching 14.6 grams compared to before treatment.

Table 2. Average blood glucose levels

Glucose (gr)	Control Negative	Control Positive	Treatment I	Treatment II	Treatment III	p value
Initial Condition	71,41 (6,21)	7 1,89 (4,51)	73,44(1,23)	67,56 (3,06)	71,96(2,80)	0,001
Pretreatment	231,75 (2,08)	232,48 (3,48)	232,33 (2,48)	233,58 (3,86)	237,30 (5,92)	
Initial DM	233,40 (1,89)	189,58 (3,07)	205,48 (2,77)	190,41 (3,18)	186,80 (1,22)	
Day 9	236,74(4,37)	132,65 (3,53)	177,42 (2,77)	142,95 (2,99)	136,97 (3,14)	
Day 15	240,54 (7,53)	117,61(1,52)	148,11(2,88)	132,68(1,77)	199,70(1,79)	
Day 21	8,79(5,45)	-114,87(1.96)	-84,22(0,4)	-100,9(-2,09)	-37,6(-4,13)	

Based on the results of measuring changes in glucose levels using the repeated ANOVA test, a p value of 0.001 was obtained so that it could be concluded that there were differences in the average blood glucose levels in each sample and there was an effect of giving Moringa leaf powder on changes in the blood glucose levels of mice. The highest reduction in glucose was achieved in the positive control group, reaching -114.87 when compared with pre-treatment in the same group. The results showed that administering Moringa leaf powder had a significant effect in reducing blood glucose levels in mice. This can be the basis for developing therapy using Moringa leaves as an alternative treatment for diabetes.

Table 3. Effect of Moringa leaf extract on changes in triglyceride levels in experimental rats

Triglyceride (gr)	Control Negative	Control Positive	Treatment I	Treatment II	Treatment III	p-value
Initial Condition	127,26 (10,18)	129,30 (4,78)	118,99(5,32)	120,41 (5,19)	131,95 (6,90)	0,001
Pretreatment	162,37 (11,05)	176,09 (9,58)	167,88 (8,08)	165,66 (10,26)	165,37 (10,86)	
Initial DM	114,20 (3,10)	83,95 (2,19)	105,30 (1,93)	98,79 (2,51)	91,02 (1,95)	
Day 9	115,98 (3,04)	80,80 (2,16)	102,00 (1,26)	93,49 (3,24)	85,78 (3,07)	
Day 15	119,01 (1,90)	73,49(2,49)	98,37(2,20)	87,91(1,62)	79,01(3,14)	
Day 21	-43,36 (-9,15)	-102,6	-69,51(-5,88)	-77,75(-8,64)	-86,36(-7,72)	

Based on Table 3, using the Repeated ANOVA test, the results showed that there was an effect of Moringa leaf extract on changes in Triglyceride levels in Experimental Rats with a p value of 0.001. The highest reduction in triglyceride levels was achieved in treatment group III, reaching -86.36 when compared to pre-treatment in the same group. These results show that Moringa leaf extract can significantly reduce triglyceride levels in experimental mice. These findings show the potential for using Moringa leaf extract as an alternative therapy to overcome the problem of high triglycerides. Apart from that, this research also shows that a significant reduction in triglyceride levels occurred after administering Moringa leaf extract for a certain period of time. This shows that regular use of Moringa leaf extract can provide benefits in reducing triglyceride levels in experimental mice.

The experimental mice used in this research were Wistar white Rattus norvegicus mice aged 8 - 12 weeks with a body weight range of 140 - 200 g, which were obtained from the Laboratory of the Center for Food and Nutrition Studies, PAU UGM Yogyakarta. The number of mice used in this study was 25, where each treatment consisted of 5 mice. The

average body weight of experimental mice at the beginning of adaptation, at the beginning of pre-treatment and at the beginning of STZ induction was 175.96 ± 9.64 grams, 179.88 ± 10.01 grams and 176.36 ± 9.98 grams. Experimental mice were selected based on age and body weight according to research criteria. The mice were obtained from the Center for Food and Nutrition Studies Laboratory, PAU UGM Yogyakarta to ensure the quality and uniformity of the mice used in this research.

The results of the statistical analysis showed that there were differences in the average body weight in the 5 times the experimental mice's body weight data were collected between the treatment groups. This means that the body weight status of experimental mice was homogeneous before treatment with Moringa leaf extract. The increase in body weight of experimental mice after being induced by STZ was shown in the positive control treatment group, treatment I, II and treatment III, while for the negative control there was a decrease in body weight in experimental mice after being induced by STZ (negative control = -14.4; positive control = 15 .2 ; P1 = 6.46 ; P2 = 13 ; P3 = 14.6).

The induction of STZ of 65 mg/kg BW and NA of 230 mg/kg BW in the 5 groups of experimental mice caused the emergence of several characteristics of diabetes mellitus such as the mice looking sick, experiencing polyuria, weight loss (negative control). In addition, mice also showed a significant increase in blood glucose levels and ketonuria. This shows that the induction of STZ and NA in the experimental group of mice succeeded in producing diabetes mellitus conditions similar to humans. After streptozotocin induction, muscle atrophy occurs accompanied by a decrease in skeletal muscle mass and loss of structural protein due to the absence of carbohydrates used in energy metabolism, resulting in weight loss. Apart from that, post-induction streptozotocin can also cause a decrease in blood glucose levels and impaired pancreatic function. This is caused by damage to the pancreatic beta cells which produce insulin, thereby disrupting glucose regulation in the body[21].

Induction of STZ in diabetic mice is associated with a characteristic loss of body weight caused by muscle wasting and due to loss of tissue protein[22]. In addition, STZ induction can also cause an uncontrolled increase in blood glucose levels, due to damage to pancreatic cells that produce insulin. This causes diabetic mice to be more susceptible to long-term complications such as kidney problems and nerve damage [23,24,25].

The weight loss of diabetic mice may be due to dehydration and increased fat and protein catabolism, leading to muscle wasting, possibly also contributing to the weight loss in diabetic mice [26,27]. In addition, increased insulin secretion can also result in increased protein synthesis due to its anabolic effect. Apart from that, increasing insulin secretion can also increase the use of glucose by body cells, reduce blood sugar levels, and inhibit fat formation. It may also contribute to weight loss in diabetic mice[28,29,30].

The decrease in the amount of insulin produced by β cells in the cells of the islets of Langerhans experienced by mice injected with STZ means that the blood glucose produced by digestion cannot be utilized by body cells [31]. The body cannot utilize glucose as an energy source, so the body uses energy reserves from protein and body fat. This causes weight loss. Apart from that, weight loss can also be caused by increasing the body's metabolism in an effort to produce enough energy. This process can cause fatigue and weakness in mice that experience a decrease in insulin levels [32].

The results of examining triglyceride levels in rats induced by Moringa leaf powder showed that there was an effect of administration in each treatment which had been tested using a statistical test which had a significant value of <0.05 in each administration of Moringa powder at different doses which had an average that reached the limit value. normal triglyceride levels. The results show that the average triglyceride levels of experimental mice at the beginning of adaptation, at the beginning of pre-treatment and at the beginning of STZ induction were 125.58 grams, 167.47 grams, 98.65 grams. The results of the examination also showed that mice given a higher dose of Moringa leaf powder had lower triglyceride levels compared to mice given a lower dose. This shows that there is a dose effect on reducing triglyceride

levels. The decrease in triglyceride levels in experimental mice showed that treatment III was very close to the normal limit, namely 110.62 mg/dl, while treatment II was 113.25 and treatment I was 118.50 mg/dl.

Diabetes mellitus sufferers will notice changes in their body metabolism, the most significant of which is related to fat, specifically increasing fat metabolism by increasing the amount of fat broken down by ketones and reducing the amount of fat in serum and triglycerides. Due to its significant lipid metabolism, diabetes mellitus is often referred to as a disorder of fat metabolism. Increased lipid metabolism in diabetes mellitus sufferers can also increase the risk of cardiovascular disease, such as stroke and heart disease. Additionally, serious cases of metabolic acidosis can be caused by increased levels of ketone bodies in the body [33]. These increased ketone levels can cause a condition called diabetic ketoacidosis, which is a potentially life-threatening complication of diabetes. Diabetic ketoacidosis occurs when the body lacks insulin, causing a buildup of ketones and a decrease in pH levels. It is important for people with diabetes to monitor their ketone levels closely and seek medical attention if they experience symptoms such as excessive thirst, frequent urination, nausea, or stomach pain.

For people with diabetes mellitus, there is a change in the conversion of glucose into fatty acids in the depot due to intracellular glucose deficiency [34]. Insulin inhibits hormone sensitive lipase in adipose tissue, and without this enzyme plasma free fatty acid levels more than double. Increased glucagon also increases fatty acid mobilization [35,36]. So, in diabetes mellitus sufferers, free fat levels in parallel with blood glucose levels are a good indicator of the severity of diabetes mellitus. Apart from that, increasing levels of free fatty acids in the blood can also cause more severe insulin resistance in people with diabetes mellitus. This can worsen blood sugar control and cause long-term complications such as heart disease and other organ damage.

Diabetes mellitus is sometimes more accurately described as a metabolic disorder resulting from impaired glucose metabolism rather than carbohydrate metabolism. Reduced metabolism in diabetes mellitus sufferers can increase the risk of kidney disease. In addition, free fatty acid levels in the blood through mealtime rituals and exercise can help increase tissue sensitivity to insulin and control diabetes. Individuals with diabetes mellitus often experience increased levels of triglycerides in their bloodstream [37]. This further supports the potential relationship between triglycerides and diabetes. Additionally, adopting a healthy lifestyle that includes regular physical activity and a balanced diet can help improve insulin sensitivity and manage diabetes effectively [38].

Under normal circumstances the body uses glucose as an energy source. In conditions of insulin resistance, hormone-sensitive lipase will become active so that triglyceride lipolysis in adipose tissue increases. This situation will produce excessive free fatty acids. Free fatty acids will enter the bloodstream, some will be used as an energy source and others will be taken to the liver as raw material for the formation of triglycerides. In the liver, free fatty acids are converted back into triglycerides and become part of VLDL. VLDL is a lipoprotein that transports triglycerides from the liver to other body tissues. Excessive VLDL production can cause fat to build up in the arteries and increase the risk of cardiovascular disease. Excessive fat buildup in the arteries can lead to atherosclerosis, a condition characterized by narrowing and hardening of the arteries. This can restrict blood flow and increase the risk of cardiovascular events such as heart attack or stroke. Therefore, maintaining a balance in VLDL production is very important to prevent cardiovascular disease [13].

The use of Moringa leaf extract has the effect of reducing triglyceride levels by 400 mg. The best dose used was 400mg in this study. The difference in triglyceride levels before and after administration of Moringa leaf extract is caused by the presence of active substances in Moringa such as alkaloids, flavonoids, tannins and saponins. This active substance has a positive effect in reducing triglyceride levels in the body. Apart from that, research also shows that consistent use of Moringa leaf extract at a dose of 400 mg can provide significant results in reducing triglyceride levels. Furthermore, the study found that a reduction in triglyceride levels was observed in participants who consistently consumed a 400 mg dose of

Moringa leaf extract over a certain period of time. This suggests that maintaining regular doses of Moringa leaf extract can lead to a sustained increase in triglyceride levels.

Moringa leaves act as antihyperlipidemia because they contain alkaloids, saponins, phytosterols, tannins, phenolics and flavonoids. Flavonoids in Moringa leaves prevent LDL oxidation and inhibit HMG-CoA Reductase activity [39]. Moringa leaves also contain vitamin C which plays a role in fat metabolism. The active compounds in Moringa leaves have very strong antioxidant activity and are able to prevent LDL from being oxidized. Apart from that, Moringa leaves also have anti-inflammatory effects which can reduce inflammation in blood vessels and prevent cardiovascular disease [40]. The phytosterol content in Moringa leaves can also help reduce cholesterol levels in the blood. In addition to its antioxidant properties, the saponins found in Moringa leaves have been shown to have potential anticancer effects [41]. This compound can inhibit the growth of cancer cells and induce apoptosis, making Moringa leaves a promising natural medicine for the prevention and treatment of cancer. In addition, the tannins in Moringa leaves are known to have antimicrobial properties, which can help protect against various bacterial and fungal infections[42].

CONCLUSION

The best dose of Moringa leaves for losing weight and reducing triglyceride levels in mice is 400 mg/kg body weight of mice. Meanwhile, the best dose to reduce glucose levels in mice is glibnclamide 0.09 mg/kg body weight of mice and Moringa leaf extract at a dose of 300 mg/kg body weight of mice. There was an effect of administering Moringa leaf extract on body weight, glucose levels, and triglyceride levels in white Wistar rats with type 2 diabetes induced by STZ (streptozotocin) with a p value of 0.001 for each variable. However, it should be remembered that the results of research on rats are not necessarily reliable. directly applied to humans. Therefore, further research and trials on humans are needed to ensure the effectiveness and safety of using Moringa leaves in reducing body weight and triglyceride and glucose levels. The next research suggestion is to conduct clinical studies involving human participants. Clinical studies may provide stronger evidence of the effectiveness of Moringa leaves in reducing body weight and triglyceride and glucose levels in humans. Apart from that, it is also important to pay attention. The implication to human health and potential side effects of consuming Moringa leaves should be thoroughly investigated. This includes monitoring any adverse reactions, assessing long-term effects, and determining the appropriate dosage for different individuals. Additionally, it would be beneficial to compare the results of Moringa leaf consumption with other existing weight loss and glucose control methods to evaluate its comparative effectiveness.

REFERENCES

1. Maresova P, Javanmardi E, Barakovic S, Barakovic Husic J, Tomsone S, Krejcar O, Kuca K. Consequences of chronic diseases and other limitations associated with old age–a scoping review. BMC public health. 2019 Dec;19:1-7.
2. Giani E, Scaramuzza AE, Zuccotti GV. Impact of new technologies on diabetes care. World journal of diabetes. 2015 Jul 7;6(8):999.
3. Hirose M, Beverly EA, Weinger K. Quality of life and technology: impact on children and families with diabetes. Current diabetes reports. 2012 Dec;12:711-20.
4. Woessner MN, Tacey A, Levinger-Limor A, Parker AG, Levinger P, Levinger I. The evolution of technology and physical inactivity: the good, the bad, and the way forward. Frontiers in public health. 2021 May 28;9:655491.
5. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Comprehensive physiology. 2012 Apr;2(2):1143.
6. Dhuli K, Naureen Z, Medori MC, Fioretti F, Caruso P, Perrone MA, Nodari S, Manganotti P, Xhufi S, Bushati M, Bozo D. Physical activity for health. Journal of Preventive

Medicine and Hygiene. 2022 Jun;63(2 Suppl 3):E150.
7. Briguglio M, Vitale JA, Galentino R, Banfi G, Zanaboni Dina C, Bona A, Panzica G, Porta M, Dell'Osso B, Glick ID. Healthy eating, physical activity, and sleep hygiene (HEPAS) as the winning triad for sustaining physical and mental health in patients at risk for or with neuropsychiatric disorders: considerations for clinical practice. Neuropsychiatric disease and treatment. 2020 Jan 8:55-70.
8. Alotaibi T, Almuhanna R, Alhassan J, Alqadhib E, Mortada E, Alwhaibi R. The relationship between technology use and physical activity among typically-developing children. InHealthcare 2020 Nov 17 (Vol. 8, No. 4, p. 488). MDPI.
9. L. J. M. Wachira, S. K. Muthuri, S. A. Ochola, V. O. Onywera, and M. S. Tremblay, "Screen-based sedentary behaviour and adiposity among school children: Results from international study of childhood obesity, lifestyle and the environment (iscole) - Kenya," *PLoS One*, vol. 13, no. 6, pp. 1–15, 2018, doi: 10.1371/journal.pone.0199790.
10. Glimcher LH, Lee AH. From sugar to fat: How the transcription factor XBP1 regulates hepatic lipogenesis. Annals of the New York Academy of Sciences. 2009 Sep;1173:E2-9.
11. Talayero BG, Sacks FM. The role of triglycerides in atherosclerosis. Current cardiology reports. 2011 Dec;13:544-52.
12. Leon BM, Maddox TM. Diabetes and cardiovascular disease: epidemiology, biological mechanisms, treatment recommendations and future research. World journal of diabetes. 2015 Oct 10;6(13):1246.
13. Gugliucci A. Triglyceride-Rich Lipoprotein Metabolism: Key Regulators of Their Flux. Journal of Clinical Medicine. 2023 Jun 29;12(13):4399.
14. Peng J, Luo F, Ruan G, Peng R, Li X. Hypertriglyceridemia and atherosclerosis. Lipids in health and disease. 2017 Dec;16:1-2.
15. Rafieian-Kopaei M, Setorki M, Doudi M, Baradaran A, Nasri H. Atherosclerosis: process, indicators, risk factors and new hopes. International journal of preventive medicine. 2014 Aug;5(8):927.
16. Tian D, Meng J. Exercise for prevention and relief of cardiovascular disease: prognoses, mechanisms, and approaches. Oxidative Medicine and Cellular Longevity. 2019 Apr 9;2019.
17. Yuan G, Al-Shali KZ, Hegele RA. Hypertriglyceridemia: its etiology, effects and treatment. Cmaj. 2007 Apr 10;176(8):1113-20.
18. Diwan AD, Ninawe AS, Harke SN. Gene editing (CRISPR-Cas) technology and fisheries sector. Canadian Journal of Biotechnology. 2017;1(2):65-72.
19. Górska-Warsewicz H, Rejman K, Laskowski W, Czeczotko M. Milk and dairy products and their nutritional contribution to the average polish diet. Nutrients. 2019 Aug 1;11(8):1771.
20. Setyawati T, Adawiyah R, Walanda RM, Chandra R. Effectiveness of moringa oleifera on triglyceride levels in diabetic wistar rats (Rattus norvegicus) induced with streptozotocin (STZ). InIOP Conference Series: Earth and Environmental Science 2022 Nov 1; 1075, (1). IOP Publishing.
21. Nakai K, Umehara M, Minamida A, Yamauchi-Sawada H, Sunahara Y, Matoba Y, Okuno-Ozeki N, Nakamura I, Nakata T, Yagi-Tomita A, Uehara-Watanabe N. Streptozotocin induces renal proximal tubular injury through p53 signaling activation. Scientific Reports. 2023 May 29;13(1):8705.
22. Cheng D, Liang B, Li Y. Antihyperglycemic effect of Ginkgo biloba extract in streptozotocin-induced diabetes in rats. BioMed research international. 2013 Jan 1;2013.
23. Martín-Carro B, Donate-Correa J, Fernández-Villabrille S, Martín-Vírgala J, Panizo S, Carrillo-López N,

Martínez-Arias L, Navarro-González JF, Naves-Díaz M, Fernández-Martín JL, Alonso-Montes C. Experimental Models to Study Diabetes Mellitus and Its Complications: Limitations and New Opportunities. International Journal of Molecular Sciences. 2023 Jun 18;24(12):10309.

24. Wang-Fischer Y, Garyantes T. Improving the reliability and utility of streptozotocin-induced rat diabetic model. Journal of diabetes research. 2018 Sep 23;2018.
25. Damasceno DC, Netto AO, Iessi IL, Gallego FQ, Corvino SB, Dallaqua B, Sinzato YK, Bueno A, Calderon ID, Rudge MV. Streptozotocin-induced diabetes models: pathophysiological mechanisms and fetal outcomes. BioMed research international. 2014 Oct;2014.
26. Patil JS, Naikawadi AA, Moharir G, Bharatha A. Effect of Glucose Tolerance Factor (GTF) on Lipid Profile, Blood Glucose Levels, and Food Intake in Streptozotocin-Induced Diabetes in Rats. Maedica. 2020 Jun;15(2):238.
27. Kifle ZD, Belayneh YM. Antidiabetic and anti-hyperlipidemic effects of the crude hydromethanol extract of Hagenia abyssinica (Rosaceae) leaves in streptozotocin-induced diabetic mice. Diabetes, Metabolic Syndrome and Obesity. 2020 Oct 29:4085-94.
28. Dilworth L, Facey A, Omoruyi F. Diabetes mellitus and its metabolic complications: the role of adipose tissues. International journal of molecular sciences. 2021 Jul 16;22(14):7644.
29. Rahman MS, Hossain KS, Das S, Kundu S, Adegoke EO, Rahman MA, Hannan MA, Uddin MJ, Pang MG. Role of insulin in health and disease: an update. International journal of molecular sciences. 2021 Jun 15;22(12):6403.
30. Karakas SE. PCOS and Insulin Resistance. A Case-Based Guide to Clinical Endocrinology. 2022:487-9.
31. Zhu BT. Pathogenic mechanism of autoimmune diabetes mellitus in humans: potential role of streptozotocin-induced selective autoimmunity against human islet β-cells. Cells. 2022 Jan 31;11(3):492.
32. Pang G, Xie J, Chen Q, Hu Z. Energy intake, metabolic homeostasis, and human health. Food Science and Human Wellness. 2014 Sep 1;3(3-4):89-103.
33. Souto G, Donapetry C, Calviño J, Adeva MM. Metabolic acidosis-induced insulin resistance and cardiovascular risk. Metabolic Syndrome and Related Disorders. 2011 Aug 1;9(4):247-53.
34. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The pathophysiology of gestational diabetes mellitus. International journal of molecular sciences. 2018 Oct 26;19(11):3342.
35. Althaher AR. An Overview of Hormone-Sensitive Lipase (HSL). The Scientific World Journal. 2022 Dec 8;2022.
36. Kojta I, Chacińska M, Błachnio-Zabielska A. Obesity, bioactive lipids, and adipose tissue inflammation in insulin resistance. Nutrients. 2020 May 3;12(5):1305.
37. Martín-Timón I, Sevillano-Collantes C, Segura-Galindo A, del Cañizo-Gómez FJ. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength?. World journal of diabetes. 2014 Aug 8;5(4):444.
38. Madhu SV. World diabetes day 2015: healthy living & diabetes. The Indian Journal of Medical Research. 2015 Nov;142(5):503.
39. Vergara-Jimenez M, Almatrafi MM, Fernandez ML. Bioactive components in Moringa oleifera leaves protect against chronic disease. Antioxidants. 2017 Nov 16;6(4):91.
40. Kashyap P, Kumar S, Riar CS, Jindal N, Baniwal P, Guiné RP, Correia PM, Mehra R, Kumar H. Recent advances in Drumstick (Moringa oleifera) leaves bioactive compounds: Composition, health benefits, bioaccessibility, and

dietary applications. Antioxidants. 2022 Feb 16;11(2):402.
41. Gopalakrishnan L, Doriya K, Kumar DS. Moringa oleifera: A review on nutritive importance and its medicinal application. Food science and human wellness. 2016 Jun 1;5(2):49-56.
42. Wu YY, Xu YM, Lau AT. Anti-cancer and medicinal potentials of Moringa isothiocyanate. Molecules. 2021 Dec 11;26(24):7512.