

## The Effect *Salvia Hispanica L* Seed Extract on Blood Sugar Levels in Rats with Moderate Physical Activity

### El efecto del extracto de semilla de *Salvia Hispánica L* sobre los niveles de azúcar en sangre en ratas con actividad física moderada

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**Abstract.** Hyperglycemia is a condition in which the body experiences an increase in the level of sugar in the blood and is a clinical manifestation of diabetes type. This unusual exercise can cause insulin resistance in patients with diabetes. Chia seeds contain a lot of antioxidants, which makes them effective in reducing oxidative stress caused by hyperglycemia and type 2 diabetes. The purpose of this study is to show the difference in the effect of the extraction of chia seeds and moderate exercise high blood sugar in T2DM. limit. and STZ injection. This research method is experimental and post-test control group design only. The number of samples is 15 male wistar rats aged 3-4 months with a weight of 180-200 grams repeated for 7 days, divided into 3 groups at random, that is the treatment group P0 as control, P1 received injection which. STZ and moderate exercise. and chia seed extract dose of 4.5 mg/kg body weight, P2 for STZ injection, for moderate exercise and chia seed extract dose of 13.5 mg/kg body weight/day. The duration of treatment is 7 days. Blood samples are taken from v. Ophthalmica on day 14. Monitor GDS level by spectrophotometer method. The data were analyzed by Anova test. The results of the study showed that the average blood sugar at P0:  $128 \pm 2.5$ ; P1:  $206 \pm 3.5$ ; P2:  $43.8 \pm 1.9$ . The results of the ANOVA test obtained a P value of 0.000 and the results of the LSD post hoc test between groups obtained a P value of 0.000 ( $<0.05$ ). The conclusion of the study is that there is an effect of giving chia seed extract doses of 4.5mg/kgBW and 13.5mg/KgBW and moderate exercise can reduce blood sugar in time.

**Keywords:** diabetes mellitus, chia seeds, blood sugar, moderate exercise

**Resumen.** La hiperglucemia es una condición en la que el cuerpo experimenta un aumento en el nivel de azúcar en la sangre y es una manifestación clínica del tipo diabetes. Este ejercicio inusual puede provocar resistencia a la insulina en pacientes con diabetes. Las semillas de chía contienen una gran cantidad de antioxidantes, lo que las hace eficaces para reducir el estrés oxidativo causado por la hiperglucemia y la diabetes tipo 2. El propósito de este estudio es mostrar la diferencia en el efecto de la extracción de semillas de chía y el ejercicio moderado con niveles altos de azúcar en sangre en la DM2. límite. e inyección STZ. Este método de investigación es únicamente un diseño de grupo de control experimental y posterior a la prueba. El número de muestras es de 15 ratas wistar macho de 3 a 4 meses de edad con un peso de 180 a 200 gramos repetidas durante 7 días, divididas en 3 grupos al azar, es decir, el grupo de tratamiento P0 como control, P1 recibió la inyección. STZ y ejercicio moderado. y dosis de extracto de semilla de chía de 4,5 mg/kg de peso corporal, P2 para inyección de STZ, para ejercicio moderado y dosis de extracto de semilla de chía de 13,5 mg/kg de peso corporal/día. La duración del tratamiento es de 7 días. Se toman muestras de sangre de v. Ophthalmica el día 14. Controle el nivel de GDS mediante el método del espectrofotómetro. Los datos fueron analizados mediante la prueba Anova. Los resultados del estudio mostraron que el nivel promedio de azúcar en sangre en P0:  $128 \pm 2,5$ ; P1:  $206 \pm 3,5$ ; P2:  $43,8 \pm 1,9$ . Los resultados de la prueba ANOVA obtuvieron un valor de P de 0,000 y los resultados de la prueba post hoc de LSD entre grupos obtuvieron un valor de P de 0,000 ( $<0,05$ ). La conclusión del estudio es que existe un efecto al administrar dosis de extracto de semilla de chía de 4,5 mg/kg de peso corporal y 13,5 mg/kg de peso corporal y que el ejercicio moderado puede reducir el azúcar en sangre con el tiempo.

**Palabras clave:** diabetes mellitus, semillas de chía, azúcar en sangre, ejercicio moderado

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### Introduction

In 2019, the International Diabetes Federation (IDF) said that at least 463 million people aged 20 to 79 worldwide have diabetes. Indonesia has the highest number of diabetics at 10.7 million and ranks 7th out of 10 countries, and is the only country in Southeast Asia to rank. Oxidative stress is a condition due to an increase in free radical production or a decrease in optimal antioxidant activity (Association, 2021). Oxidative stress in the body can lead to various diseases such as atherosclerosis, diabetes, and arthritis. The hyperglycemic condition in DM will aggravate the formation of ROS that increases endothelial cell apoptosis in vitro and in vivo such that it shows an

increase in free radicals and a decrease in antioxidant capacity. Oxidative stress in people with diabetes can arise due to lipid glycation and oxidation reactions, which will lead to an imbalance between antioxidants and oxidants in plasma cells, thereby increasing the formation of ROS (Ayerza, 2004; Nasrulloh et al., 2021). To avoid the accumulation of oxidative stress and hyperglycemia, it is important to eat foods high in antioxidants, including chia seeds (*Salvia Hispanica L.*).

Research on chia seeds is still very limited. In 2017, a study by Vuksan et al showed that the administration of chia seeds in the treatment of patients with type 2 diabetes caused a decrease in blood sugar levels after fasting in patients with type 2 diabetes mellitus. and rats with

diabetes (Ayerza, 2005; Yudhistira et al., 2021). Studies by Anastasia., et al., have shown chia seeds to reduce LDL levels, total cholesterol, triglycerides, but have no effect on increasing HDL levels. It is suspected that the dose is not variable, so the dose is not effective in raising HDL levels. A dose of 42.5 g/kg was ineffective in raising HDL levels. Research should be done on more effective dosage regimens such as 4.5mg/oral and 13.5mg/oral should show a reduction in LDL, total cholesterol, triglycerides, increased HDL and decreased TNF $\alpha$  levels. The results of the research by Anastasia., et al showed that the HDL results of the P0 group were higher than those of the P1, namely  $25.22 \pm 0.37$  mg/dl compared to  $16.16 \pm 2.43$  mg/dl ( $p < 0.01$ ).

Chia seeds are another source of potential food product development as a natural health supplement (Ayerza, 2015; Nasrulloh et al., 2022). Conducted research by processing chia seeds into flour and treating pre-diabetic rats. The findings of this study showed that chia seeds can reduce glucose levels and restore stability (Ayerza, 2017; Kristiyanto et al., 2020). in the case of intestinal obstruction. Chia seeds contain phenolic compounds that include flavonols and phenolic acids (myricetin, quercetin, kaempferol, caffeic acid) (Badan Litbang Kesehatan, 2018; Listyarini et al., 2021). These phenolic compounds are the main synergistic antioxidants with high antioxidant activity from chia seeds, including quercetin. Quercetin is a powerful antioxidant compound that can prevent the oxidation of fats, proteins, and DNA and has a more effective antioxidant capacity than other flavonoid compounds (Safari et al., 2016; Sukendro et al., 2021).

Antioxidants are a new focus in efforts to control coronary heart disease (CHD) risk, as these drugs are inexpensive and safe. Treatment and prevention of disease with antioxidants is a treatment that is not inferior to drugs or lifestyle (Muhammed, 2023; Ilham et al., 2021). It has been proven that powerful antioxidants can fight many diseases, even devastating diseases that are not easy to treat. In nature, there are things people can eat to prevent free radicals (Herbert-Doctor et al., 2023). One of the free radical blockers is chia seeds. Many people are not familiar with chia seeds. This type of corn is found in Mexico and Guatemala. Chia seeds contain omega 3 ALA (alpha-linolenic acid) (Baynes & Dominiczak, 2015; Sutapa et al., 2021). Also, chia seeds are rich in fiber, vitamins and minerals. Due to their high antioxidant content, chia seeds have benefits such as reducing triglyceride and cholesterol levels, which can reduce blood pressure and heart disease. Moreover, it can also act as an anti-inflammatory, cardioprotector and hepatoprotector, antidiabetic, protection against arthritis, autoimmune diseases and cancer. Flavonoids are one of the antioxidants found in chia seeds (Diyah, 2014) (Radica Dragojlovic Ruzicic, 2016)

A study conducted in China with 217 samples showed that treatment with subcutaneous subcutaneous infusion (CSII) and CSII-sitagliptin combination had an effect on glycemic control and prevented the second complication of

type 2 diabetes. Also, the use of CSII-sitagliptin combination had an effect. greater effect than using CSII monotherapy. Treatment using ADO and Insulin According to BPJS data, the amount spent on diabetes treatment in 2018 was Rp. 6.1 trillion, diabetes mellitus is a chronic disease with the highest cost of Rp. 6.1 trillion, about 87.5% is used to treat patients suffering from diabetes. complicated ones, only about 0.5% is used to buy drugs. This shows the large amount of government spending for the management of diabetes mellitus in Indonesia. The Diabetes Prevention Group shows that at least one hundred and fifty minutes per week of moderate intensity exercise as part of a lifestyle can significantly reduce the development of type II diabetes.

Endurance (aerobic) exercise can reduce hemoglobin (HbA1c) glycosylation in type II diabetes by approximately 0.66%, an amount expected to reduce the risk of diabetes complications (Baynes & Dominiczak, 2015; Kogoya et al., 2023). In 2017, a study conducted by Vuksan et al showed that the administration of chia seeds in the treatment of patients with type 2 diabetes mellitus led to a decrease in blood sugar levels after fasting in patients with diabetes (Radica Dragojlovic Ruzicic, 2016). Chia seeds or chia seeds (*Salvia hispanica L.*) are another source for the development of potential food products as natural health products (Enes et al., 2020).

In a previous study by Diyah et al, it was found that there was no significant relationship between plasma glucose levels and renal MDA levels in a group of STZ-induced mice. This study will investigate the effect of chia seed extract on GDS levels in moderately exercising male Wistar rats (Reyes-Caudillo et al., 2008). The parts of this book are organized as follows: the first part deals with the revision of the introduction. Section 2 reviews the overall findings and methods, Section 3 presents the results, Section 4 presents the discussion of the study and finally Section 5 concludes the results of the study.

## Materials and Methods

This research is an true experimental study using a post-test control group sample. The Research Center of Biology and Chemistry Laboratory of IBL FK Unissula The research period is conducted for 3 months from August 2022 to October 2022. Independent change of chia seeds at a dose of 4.5 mg / kg body weight and 13.5 mg / kg of body weight in the macerated method, the change depends on the blood sugar at that time. Inclusion criteria male wistar rat, age 3-4 months, weight 180-200 grams and healthy. Dropout criteria mice wouldn't eat and got sick or died in the study.

The number of groups in this study is 3 groups, group 1 is the control group, groups 2 and 3 are the groups that received chia seeds and received moderate exercise in each group, there is a limit 5 which is left and chosen based on it. exclusion and inclusion criteria. A sample of 15 rats was reconditioned for one week before treatment. All eligible

mice will be included in the study sample. Ten Wistar rats were recruited and randomly divided into three groups, each group containing five rats. Group 1 was a control group, group 2 was a treatment group with 13.5 mg/kg body weight of chia seeds, and group 3 received moderate exercise. This research has received approval from Unissula School of Medicine Bioethics Commission Ethics Clearance Number 18/1/2022/Bioethics Commission. Look for a method :

1. Selection of 15 white rats of the Wistar breed (*Rattus Norvegicus*) aged 3-4 months and weighing about 180-200 grams.

2. Rats were acclimated for approximately one week and fed a standard diet in the form of HBS pellets ad libitum.

3. The mice are placed in the cage with the requirements as a research study, that is, the mice are placed in a plastic cage, measuring 30 x 20 x 20 cm and covered sand and wire insulation. The holes are placed in an air-conditioned room with natural ventilation. In 1 point put 6 limits.

4. Extraction process of Chia seeds: The process of ethanolic extraction of Chia seeds is carried out in the chemical laboratory of FK UNISSULA Semarang. Simplicia was dried in a 400 °C oven for 7 hours to 1500 grams of crushed and processed chia seeds, which were extracted in 7.5 liters (1:5) of 70% ethanol using the maceration method and agitated with an agitator for 1 hour. , and leave for 24 hours. The macerate is checked and separated using a flannel cloth. The macerate is removed using a rotary pump under vacuum at a temperature of 40 ° C. and a speed of 100 rpm. The viscous drag is calculated and the result measured.

5. When group 1 as a control received a standard diet, group 2 received streptozotocin induced and induced streptozotocin and received chia seeds to remove 13.5mg / kg body weight and moderate exercise, the induction of streptozotocin was selected by using the injection method because the sample will not be permanent. forget that treatment is done and reduce if streptozotocin is given immediately sometimes only 1 or 2 samples are treated so as not to discriminate.

6. Treatment given: P0 treatment and control group only with standard food. Group P1 received an injection of 35 mg/kg of streptozotocin, then 4.5 mg/kg of chia seed extract for 7 days and moderate exercise in the form of swimming every morning with an intensity of 15 minutes for 7 days. P2 received 35 mg/kg of streptozotocin, then 13.5 mg/kg of chia seed extract for 7 days and moderate exercise in the form of swimming every morning at a strength of 15 minutes for 7 days.

7. After treatment, check the GDS level as post-test.

8. Take 1 cc of blood from the medial canthus of the orbital sinus and a mixture of ketamine - xylazine anesthesia 40 - 80 mg/kgBB (k) intraperitoneal and 5 - 10 mg / kgBB (x) intraperitoneal.

9. After the search, the mice will be deleted. Average blood sugar level data when presented in a table or graph.

Data were tested with the Kolmogorof Smirnof test to show normality and Levene's test to show homogeneity. If the result is normal in one group, we proceed with the one-way ANOVA test. If the result of the one-way ANOVA test is  $p < 0.05$ , this means that there is a difference from one group to another and the other , followed by Post Hoc. Try the LSD test. If the data is not normal in one way or the other, the one-way Anova test does not meet the requirements and the data is tested using the Kruskal Wallis test (a non-parametric test) if the results the Kruskal Wallis test is  $p < 0.05$ , it means that there is a difference between the groups and to see the difference they are tested with a different test. Mann Whitney.

## Results

The research was conducted for three months at FK UNISSULA Semarang Integrated Biomedical Laboratory. During treatment, no rats died and all met the inclusion criteria. No mice stopped until the end of the study. Then, on day 14, blood sugar levels were monitored in male wistar rats that had been injected with STZ. In this study, there are 3 groups that make up the P0 group, i.e. the control group that received only the standard diet, group P1, that is the group that received STZ injection of 55mg/kgBB for 3 days, followed by chia seeds. 4.5 mg/kgBB/day for 7 days and subjected to moderate exercise by swimming 15 minutes daily. Group P3, that is the group that received STZ injections of 55 mg/kg for 3 days, then continued with 13.5 mg/kg/day of chia seeds for 7 days and received moderate exercise by swimming for 15 minutes a day.

From table 1 and figure 1, it can be seen that the mean glycemia at P0:  $128 \pm 2.5$  mg/dL; P1:  $206 \pm 3.5$ mg/dL; P2:  $43.8 \pm 1.9$  mg/dL. The average blood sugar level in P1 is higher than P0, P2, but in P2 it is the lowest compared to P0, P1. The data is analyzed using parametric statistics, namely the Anova test as the data distribution is normal and uniform. The results of the analysis using the ANOVA test obtained a p-value of 0.000, which means that there is a significant difference in the blood sugar levels in the three groups.

To identify significantly different groups, post hoc LSD tests were performed as described below.

The results of the LSD post hoc test in Table 2 show that there is a significant difference in the mean blood glucose levels in the P0 and P1 groups ( $p=0.000$ ); P0 and P2 ( $p=0.000$ ); P1 and P0 ( $p=0.000$ ); P1 and P2 ( $p=0.000$ ); P2 and P0 ( $p=0.000$ ); P2 and P1 ( $p=0.000$ ). Based on the above data, it can be concluded that the administration of chia seeds and moderate exercise affects the reduction of blood sugar levels in Wistar rats injected with streptozotocin.

In Figure 1 it is explained that the mean blood sugar levels during each of the PO, P1, and P2 groups. P2 shows the lowest average number compared to PO and P1. In table 2 are the results of the post hoc test on random blood sugar

levels with a value of  $p = 0.000$  in each comparison of groups P0 to P1 and P2, P1 to P0 and P2 and P2 to P0 and P1.

Table 1.

The results of the analysis of the average blood glucose over time				
Variable groups	P0 N=5 Mean±SD	P1 N=5 Mean±SD	P2 N=5 Mean±SD	Sig.(p)
Blood sugar level (mg/dL)	128±2.5	206±3.5	43.8±1.9	
Shapiro wilk	0.69*	0.84*	0.92*	
Levene test				0.303**
Anova				0.000***
Description:				
Normal		*	>0.05	
Homogen		**	>0.05	
There is a significant difference between groups		***	<0.05	

Table 2.

Data Anova				
Group	P0	P1	P2	
P0	-	0.000	0.000	
P1	0.000	-	0.000	
P2	0.000	0.000	-	

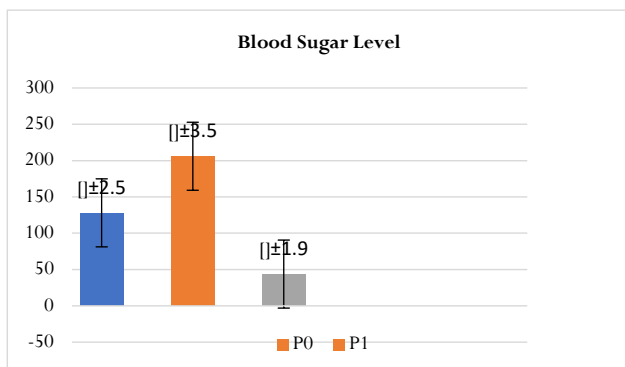


Figure 1. Average Blood Sugar Levels During

## Discussion

In this study, two doses of chia seeds were given, namely in P3 group with a dose of 4.5 mg/kg of chia seeds and in group P4 with a dose of 13.5 mg/kg of say seed. After giving chia seeds daily for seven days, we obtained post hoc results on GDS level analysis which showed significant results for both groups. Chia seeds are a nutritious food with high fiber content and a high content of free fatty acids, proteins, minerals, vitamins and phenolic compounds that can stabilize blood sugar levels in people with diabetes (Evi & Yanita, 2016). In a study conducted by Barbara et al, extracting chia seeds into chia oil can significantly reduce blood glucose levels. Consumption of chia seeds was associated with restoration of lipid and restoration of FAT/CD36 in the plasma membrane, mitochondrial function and beta-oxidation (Gumantara & Oktarlina, 2017). The distribution of lipids will increase glucose tolerance due to the reduction of body adiposity due to its association with ALA consumption. ALA is an activator of AMPK, the activation of AMPK will reduce blood glucose levels by phosphorylating protein AS160 which is a protein that is active in glucose transporters, increasing the absorption of glucose in a way that depends on insulin. Chia seeds themselves can increase AMPK expression in the liver, so AMPK can increase glucose

uptake and oxidation, as well as glycolytic enzymes, resulting in increased glucose (Husna et al., 2019). A study by Fonte-Feria et al in mice fed a HFD showed that chia seeds can restore glucose and insulin tolerance. In a study conducted by Vukasa et al, (2007), said that chia seeds can maintain good glycemic and lipid control in type 2 diabetes that is well controlled. Chia fruit is a plant rich in antioxidants, its composition includes vitamin C, vitamin E, carotenoids, phenolic compounds and polyphenols that can be in the form of flavonoids (v. Vuksan, 2016). Flavonoids with antioxidant activity include flavones, flavonols, isoflavones, catechins, flavonols and chalcones, micronutrients found in plants such as vitamins A, C, E, folic acid, carotenoids, anthocyanins and polyphenols have the ability to avenge free radicals so they can (Willems et al., 2023). To be used as a substitute for the consumption of synthetic antioxidants (Dragojlovic Ruzicic et al., n.d.). In a previous study by Diyah et al, it was found that there was no significant relationship between plasma glucose levels and renal MDA levels in a group of rats that did or did not receive STZ exercise. that is always considered (Diyah, 2014).

In type 2 diabetes, hyperglycemia is an underlying condition that can lead to increased insulin resistance and/or pancreatic  $\beta$ -cell proliferation. Hyperglycemia in type 2 DM worsens the production of free radicals so that oxidative stress increases and increases the risk of disease complications (IDF Atlas 10th Edition 2021, 1976).

Hyperglycemia is a condition characterized by high blood sugar (blood sugar), high blood sugar occurs when the body has too little insulin or when the body cannot use insulin properly. In DM, the increase in blood sugar indicates an increase in the level of GDS  $\geq 200$  mg / dL, GDP  $\geq 126$  mg / dL, HbA1c  $\geq 6.5\%$ , blood sugar 2 hours after OGTT  $\geq 200$  mg/dL. This condition causes the body to need antioxidants, antioxidant deficiency can occur in type DM 2 which will cause metabolic problems such as hyperlipidemia, hyperglycemia, hyperinsulinemia with toxic effects on macrovascular and microvascular. A decrease in the level of antioxidants in the body and an increase in free radicals in the body will lead to oxidative stress that can lead to cell and tissue damage, such as a decrease in endothelial nitric oxide synthesis (NO), a decrease in vascular antioxidant protection and other factors. Again (PERKENI, 2020).

The intervention of providing antioxidants and moderate exercise in the process of WHO in people with DM can restore the endothelial function that occurs due to insufficient antioxidant protection, this can be achieved by providing antioxidant food. The role of antioxidants is to prevent and neutralize the oxidation reaction associated with free radicals. obtaining and neutralizing free radicals or destroying peroxides (Prawitasari, 2019).

Physical activity is a key factor in the management of type 2 diabetes. Regular exercise is performed 3-5 days per week for approximately 30-45 minutes, for a total of 150 minutes per week, with breaks in 'the center of exercise is less than 2. in the order of days. Daily activities or

daily activities are not included in the exercise. Exercise, in addition to maintaining good health, can also lead to weight loss and improve insulin sensitivity, which will improve blood sugar control. Recommended exercise is moderate-intensity aerobic exercise (50-70% of heart rate) such as brisk walking, recreational cycling, jogging and swimming. The maximum heart rate was calculated by subtracting 220 from the patient's age. Young, fit diabetics can do 90 minutes/week of vigorous exercise, reaching >70% of heart rate. It is recommended to check blood sugar before exercise. Patients with blood glucose <100 mg/dL should eat carbohydrates first and if >250 mg/dL, it is recommended to postpone exercise. Asymptomatic diabetics do not need special medical evaluation before they start light to moderate exercise, such as brisk walking. People who are going to do high intensity exercise or who meet high risk should go for medical examination and physical examination before exercising (Nugroho, 2012; Nurul, 2012; Prawitasari, 2019).

In DM patients without contraindications (eg osteoarthritis, uncontrolled hypertension, retinopathy, nephropathy) it is recommended to do strength training (weight training) 2-3 times a week as prescribed by the doctor. Exercise should be modified according to age and physical condition. Vigorous exercise in DM patients who are relatively healthy can be increased, while in DM patients with complications, exercise should be reduced and adjusted for each individual (V. Vuksan et al., 2017).

## Conclusions

The conclusion of this study is that the effect of the combination of chia seed extract administration and moderate exercise can reduce blood sugar in male wistar rats with streptozotocin injection. Moderate physical activity acts as a factor in lowering blood sugar in patients with type 2 diabetes mellitus. The combination of antioxidant chia seeds with moderate physical activity gives satisfactory results for lowering blood sugar levels in type 2 diabetes.

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## Conflict of interest

All authors know of no conflict of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome. As corresponding author, Reza Adityas Trisnadi confirmed that the manuscript has been read and approved for submission by all the named authors.

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