

Effect of Chia Seed Extract (*Salvia Hispanica L*) On Current Blood Sugar Levels and MDA Levels Efecto del extracto de semilla de chíá (*Salvia hispánica L*) sobre los niveles actuales de azúcar en sangre y los niveles de MDA

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Abstract. Hyperglycemia is a condition in which the body experiences an increase in blood sugar levels and is a clinical manifestation of type 2 DM which will increase ROS so that an antioxidant imbalance occurs which results in oxidative stress, one of the biomarkers, namely MDA. Chia seeds contain high antioxidants so that they are effective in reducing oxidative stress caused by hyperglycemia in type 2 diabetes. The research study was to prove the effect of chia seed extract on GDS and MDA levels in DMT2 rats with STZ injection. The methods is experimental research with Posttest Only Control Group Design. The number of samples was 25 male wistar rats aged 3-4 months with a weight of 180-200 grams and adapted for 7 days, divided into 5 groups randomly, namely the treatment group P0 as a control, P1 as a positive control, P2 as a negative control, and P3 as a control group. STZ injection and chia seed extract at a dose of 4.5 mg/KgBW/day, P4 for STZ injection and chia seed extract at a dose of 13.5 mg/KgBW/day. Treatment time is 7 days. Blood samples were taken from v. Ophthalmica on day 14. Examination of GDS levels using the ELISA method and examination of MDA levels using the TBARS method, the data were analyzed by the Anova test. The result Mean level of GDS P0: 127.6 ± 2.8 ; P1: 204.6 ± 6.1 ; P2: 76.2 ± 1.3 ; P3: 45.6 ± 2.07 ; P4: 40 ± 1.58 . Mean levels of MDA in nmol/ml P0: 0.93 ± 0.04 ; P1: 1.20 ± 0.01 ; P2: 0.73 ± 0.04 ; P3: 0.44 ± 0.03 ; P4: 0.22 ± 0.20 . The results of the ANOVA test obtained a P value of 0.000 and the results of the post hoc LSD test between groups obtained a P value of 0.000 (< 0.05). conclusion is significant difference in reducing GDS and MDA levels between Chia seed extract doses of 4.5 mg/KgBW/day and 13.5 mg/kgBW/day.

Keywords: chia seeds; MDA; GDS; DM Type 2

Resumen. La hiperglucemia es una condición en la que el cuerpo experimenta un aumento en los niveles de azúcar en sangre y es una manifestación clínica de la DM tipo 2 que aumentará las ROS de modo que se produzca un desequilibrio antioxidante que resulta en estrés oxidativo, uno de los biomarcadores, a saber, MDA. Las semillas de chíá contienen altos niveles de antioxidantes, por lo que son eficaces para reducir el estrés oxidativo causado por la hiperglucemia en la diabetes tipo 2. El estudio de investigación tuvo como objetivo demostrar el efecto del extracto de semilla de chíá sobre los niveles de GDS y MDA en ratas DMT2 con inyección de STZ. El método es una investigación experimental con diseño de grupo de control únicamente posprueba. El número de muestras fue de 25 ratas wistar macho de 3-4 meses de edad con un peso de 180-200 gramos y adaptadas durante 7 días, divididas en 5 grupos aleatoriamente, a saber, el grupo de tratamiento P0 como control, P1 como control positivo, P2. como control negativo, y P3 como grupo de control. Inyección de STZ y extracto de semilla de chíá a dosis de 4,5 mg/KgPV/día, P4 para inyección de STZ y extracto de semilla de chíá a dosis de 13,5 mg/KgPV/día. El tiempo de tratamiento es de 7 días. Se tomaron muestras de sangre de v. Ophthalmica el día 14. Examen de los niveles de GDS mediante el método ELISA y examen de los niveles de MDA mediante el método TBARS, los datos se analizaron mediante la prueba Anova. El resultado Nivel medio de GDS P0: $127,6 \pm 2,8$; P1: $204,6 \pm 6,1$; P2: $76,2 \pm 1,3$; P3: $45,6 \pm 2,07$; P4: $40 \pm 1,58$. Niveles medios de MDA en nmol/ml P0: $0,93 \pm 0,04$; P1: $1,20 \pm 0,01$; P2: $0,73 \pm 0,04$; P3: $0,44 \pm 0,03$; P4: $0,22 \pm 0,20$. 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 es una diferencia significativa en la reducción de los niveles de GDS y MDA entre dosis de extracto de semilla de chíá de 4,5 mg/kg de peso corporal/día y 13,5 mg/kg de peso corporal/día.

Palabras clave: semillas de chíá; MDA; GDS; DM tipo 2

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Introduction

Indonesia has a number of diabetics of 10.7 million and is ranked 7th out of 10 countries, and the only country from Southeast Asia that is included in the ranking. The prevalence of patients with diabetes in Indonesia reaches 6.2 percent, which means that there are more than 10.8 million people suffering from diabetes per year 2020. General Chair of the Indonesian Endocrinology Association (Perkeni), Prof. Dr. Ketut Suastika SpPD-KEMD said that this figure is estimated increase to 16.7 million patients per year 2045. With data for 2020, 1 in 25 Indonesians or

10 percent of Indonesians have diabetes. Based on the 2018 Basic Health Research (RISKESDAS), the prevalence rate of diabetes in Indonesia has reached 10.9 percent which is predicted to continue to increase. The number of Diabetes Mellitus sufferers in Indonesia based on Riskesdas data for 2018 by the Ministry of Health showed an increase of 1.6% from 2013 to 2018 with a total of approximately 4 million sufferers (Kesehatan et al., 2020).

Oxidative stress is a condition caused by increased free radical production or reduced antioxidant activity. Oxidative stress on tissues can give rise to various diseases such as atherosclerosis, diabetes, rheumatic arthritis. Hyperglycemia

in DM will worsen the formation of ROS which has increased endothelial cell apoptosis in vitro and in vivo, thus showing an increase in free radical formation and a decrease in antioxidant capacity (Prawitasari, 2019). Oxidative stress in people with DM can occur due to glycation and lipid oxidation reactions which will result in an imbalance between antioxidants and oxidants in cell plasma, thereby increasing the formation of ROS (Hendriyani, 2018).

To prevent the accumulation of oxidative stress and high blood glucose levels, it is necessary to consume nutrients with a fairly high antioxidant content, one of which is a plant with a relatively high antioxidant content, chia seeds (*Salvia Hispanica L.*). Research on chia seeds is still very limited. In 2017 a study conducted by Vuksan, et al showed that the administration of chia seed extract in the treatment of type 2 DM patients found a decrease in blood sugar levels after fasting in type 2 DM patients. It is necessary to conduct research on chia seeds on blood sugar levels during and MDA levels in mice that experienced DM (v. Vuksan, 2016).

Chia seeds are an alternative to the development of food products that have the potential to be natural ingredients in health (Safari et al., 2016). Conducted a study by making chia seeds into flour and treating rats that had previously been made to suffer from diabetes the results shown from the study that chia seeds can reduce glucose levels and can restore the integrity of the intestinal barrier (Beltrán-Orozco et al., 2020). Chia seeds have phenol component compounds consisting of flavonols and phenolic acids (myricetin, quercetin, kaempferol, caffeine acid) (Grancieri et al., 2019; Marineli et al., 2015). The compounds of the phenol component are a primary and synergistic antioxidant that has an impact on the proportion of high antioxidant activity derived from chia seeds, one of these compounds is quercetin. Quercetin is a powerful antioxidant compound that is able to prevent the oxidation of fats, proteins and DNA and has antioxidant capabilities that are more effective than other flavonoid compounds (V. Vuksan et al., 2017). This study will look at the effect of chia seed extract on GDS levels and MDA levels in male rats of the wistar strain.

The purpose of this study was to determine the effect of chia seed extract (*Salvia Hispanica L.*) on transient blood sugar levels and MDA levels in STZ-induced Wistar male rats.

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 type of research is experimental using a research design, namely Post-test only Control Group Design. This research was conducted at the Integrated Biomedical Laboratory of FK Unissula, biology and chemistry section of the Faculty of Medicine, Sultan Agung Islamic University. The

research was carried out for 3 months from January 2022 to June 2022. The study population was male rats of the wistar strain obtained from Java Rat Labs Semarang. Rats are kept with standardized pellet feed and drinking water in the form of maintenance room temperature aqueous ranging from 28° – 32°C with sufficient ventilation and room. The rats were then adapted for 1 week before being treated. The sample of this study used was 5 male wistar mice per group so the total sample size was 25 male wistar rats. The administration of chia seed extract (*Salvia Hispanica L.*) dose 4.5 mg / kgBB / day and 13.5 mg / kgBB / day is a free variable, Blood sugar levels while and MDA levels are dependent variables. Chosen Foods Organic chia seeds are bought in supermarkets and are a type of grain derived from plants of the mint (*Labitae*) group. This chia seed extract was given to rats for 7 days. The dose was 4.5 mg/kgBB/day and 13.5 mg/kgBB/day. Made by means of maceration extrasion. Malondialdehyde is the end result of lipid peroxidation. MDA levels were examined from blood samples taken through the medial cantus sinus orbitalis on day 7 using the TBARS method read on a wavelength spectrophotometer λ 532 nm with mmol / ml units. Blood Sugar Sewaktu (GDS) is a measurement of blood glucose levels that can be taken at any time indefinitely, and without considering the time of consumption of the last meal. The levels obtained from GDS animal blood taken as much as 0.5 cc from sinus orbita, blood centrifused for 15 minutes and serum taken then read using a wavelength spectrophotometer λ 532 nm. Glucose reagent kit. The normal value of glucose when it is < 180 mg/dL. Streptozotisin is a drug that can induce diabetes through damage to pancreatic beta cells. STZ was injected intraperitoneally at a dose of 40-55 mg/kg BB in rats and 180-200 mg/kg BB in rats. Samples were randomly taken as many as 25 mice and then adapted first for 1 week before being treated. All mice that had successfully met the inclusion criteria were included in the study sample. Twenty-four male wistar rats were taken and divided into 5 groups randomly, each group had 5 mice. Group 1 as a control, group 2 as a negative control induced by STZ and standard feed, group 3 as a positive control group that was STZ induced and given metformin (500 mg converted to a rat dose to 9 mg/mL), group 4 as a treatment group with STZ and administration of chia seed extract dose 4.5 mg/kgBB/day, and group 5 as a treatment group with high cholesterol feed and a dose of chia extract of 13.5 mg/kgBB/day. Etichal clearance No.18/I/2022/Bioethics Commission issued on January 31, 2022. The average data of current blood sugar levels and MDA levels are presented discriptively in the form of a table or graph. The data were tested with the Shapiro Wilks test to show normality and the Levene test to show homogeneity. Normal and homogeneous data results continued with the One Way Anova test, the one way anova p test result < 0.05 means that there is a difference between one group and another, followed by the Post Hoc LSD test.

Results

This research was conducted for 2 weeks at the Integrated Biomedical Laboratory FK UNISSULA Semarang. During the treatment no rats died and all met the inclusion criteria. No rats dropped out until the end of the study. Then on day 14, blood sugar levels and MDA levels were checked in male rats of the wistar strain injected with STZ.

Based on Table 4.1 and graph 4.1 shows that the average blood sugar level while at P0: 127.6±2.8 mg/dL; P1 : 204.6±6.1 mg/dL; P2 : 76.2±1.3 mg/dL; P3 : 53.4±2.4 mg/dL; P4: 41.2±1.3 mg/dL. The average blood sugar level at P1 is higher than that of P0, P2, P3 and P4, but at P4 it is lowest when compared to P0, P2, and P3. Anova test due to normal and homogeneous data distribution. The results of the analysis with the Anova test obtained a p value of 0.000, meaning that there was a significant difference in the average blood sugar levels in all 5 groups. The results of the LSD post hoc test in table 4.2 showed that there was a significant difference in the average blood sugar levels in the P0 and P1 groups (p=0.000); P0 and P2 (p=0.000); P0 and P3 (p=0.000); P0 and P4 (p=0.000); P1 and P2 (p=0.000); P1 and P3 (p=0.000); P1 and P4 (p=0.000); P2 and P3 (p=0.000); P2 and P4 (p=0.000); P3 and P4

(p=0.000). Based on the data above, it can be concluded that the administration of chia seed extract has a significant effect on reducing blood sugar levels while in male rats of the wistar strain injected with STZ.

Based on Table 1 and graph 2 shows that the mean MDA levels at P0: 0.93±0.04 mg/dL; P1 : 1.20±0.0019 mg/dL; P2 : 0.73±0.043 mg/dL; P3 : 0.44±0.03 mg/dL; P4: 0.22±0.20 mg/dL. The average MDA level at P1 is higher compared to P0, P2, P3 and P4 but at P4 it is lowest when compared to P2, P3 and P0. the Anova test obtained a p value of 0.000, meaning that there was a significant difference in the average MDA levels in all 5 groups. The results of the post hoc LSD test in table 3 showed that there was a significant difference in the average MDA levels in the P0 and P1 groups (p=0.000); P0 and P2 (p=0.000);

P0 and P3 (p=0.000); P0 and P4 (p=0.000); P1 and P2 (p=0.000); P1 and P3 (p=0.000); P1 and P4 (p=0.000); P2 and P3 (p=0.000); P2 and P4 (p=0.000); P3 and P4 (p=0.000). Based on the data above, it can be concluded that the administration of chia seed extract has a significant effect on reducing MDA levels in male rats of the wistar strain injected with STZ.

Table 1. Results of the analysis of the average blood sugar level during and MDA levels

Group Variable	P0 N=5 Mean±SD	P1 N=5 Mean±SD	P2 N=5 Mean±SD	P3 N=5 Mean±SD	P4 N=5 Mean±SD	Sig.(p)
Current Blood Sugar Levels (mg/dL)	127.6±2.8	204.6±6.1	76.2±1.3	53.4±2.4	41.2±1.3	
Shapiro wilk	0.74*	0.08*	0.42*	0.78*	0.42*	
Levene test						0,108**
Anova						0,000***
Up to MDA (nmol/dL)	0.93±0.04	1.20±0.01	0.73±0.04	0.44±0.03	0.22±0.20	
Shapiro wilk	0.28*	0.92*	0.41*	0.41*	0.75*	
Levene test						0.150**
Anova						0.000***

Information:		
Normal	*	>0.05
Homogeneous	**	>0.05
Significant differences between groups	***	<0.05

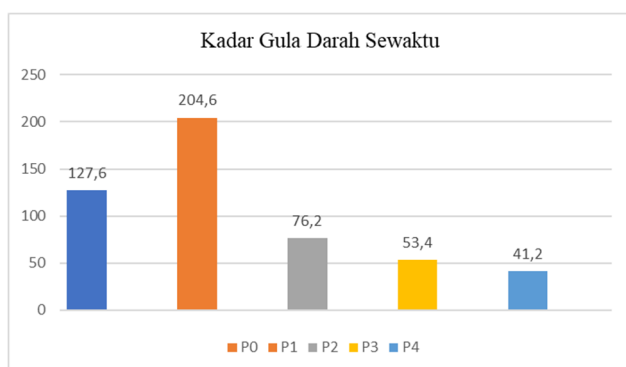


Figure 1. Average blood sugar levels during

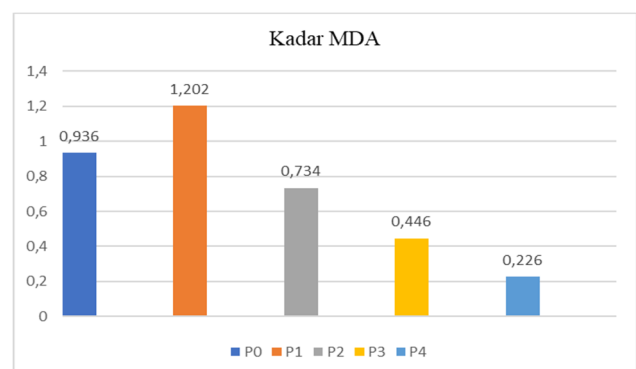


Figure 2. Average MDA Levels

Table 2. Post Hoc Test Results Mean Blood Sugar Levels During

Group	P0	P1	P2	P3	P4
P0	-	0.000	0.000	0.000	0.000
P1	0.000	-	0.000	0.000	0.000
P2	0.000	0.000	-	0.000	0.000
P3	0.000	0.000	0.000	-	0.000
P4	0.000	0.000	0.000	0.000	-

Table 3. Post Hoc Test Results Mean MDA Levels

Group	P0	P1	P2	P3	P4
P0	-	0.000	0.003	0.000	0.000
P1	0.000	-	0.000	0.000	0.000
P2	0.000	0.000	-	0.000	0.000
P3	0.000	0.000	0.000	-	0.000
P4	0.000	0.000	0.000	0.000	-



Figure 3. Sampling process

Figure 4. Evaporation process



Figure 5. Chia Seeds

Discussion

This study also administered chia seed extract using two doses, namely in the P3 group with a chia seed dose of 4.5 mg / kgBB and the P4 group with a chia seed dose of 13.5 mg / kgBB after seven days after giving chia seed extract, so an MDA level examination was also carried out which showed post hoc results in the P3 and P4 groups there was a significant decrease. The administration of chia seed extract succeeded in reducing the average blood sugar level while with the results of the chia seed dose of 4.5 mg / KgBB which was 53.4 ± 2.4 , the dose of chia seeds was 13.5 mg / KgBB which was 41.2 ± 1.3 and a significant difference was obtained between the P0, P1, P2, P3 and P4 groups.

Chia seeds are a food source that contains a lot of fiber with a high content of unsaturated fatty acids and protein free of gluten, minerals, vitamins, and phenolic compounds that can stabilize blood glucose levels in DM patient (Sharma et al., 2018). In a study conducted chia seeds Ekstrak process extracted into chia oil can significantly reduce blood glucose levels (Enes et al., 2020). Chia seeds themselves can increase the expression of AMPK in the liver, so that AMPK can increase the absorption and oxidation of glucose, as well as the enzyme glycolysis, resulting in an increase in glucose tolerance (Haros et al., 2015). Research conducted by Fonte-Feria, et al in mice fed the HFD diet showed results that chia seeds can restore glucose and insulin tolerance (Marineli et al., 2015). In a study conducted by Vukasa, et al stated that chia seeds can maintain good glycemic and lipid control in well-controlled type 2 diabetes (V. Vuksan et al., 2017).

In measuring MDA levels, the highest MDA levels in the

P1 group were obtained, this STZ will destroy pancreatic β cells to cause damage to cells and body tissues which will later cause a death of body tissue cells, while nicotinamide will provide a protective effect and repair the entire body's metabolic system so as to increase the survival rate (Cruz et al., 2021). In the group given metformin experienced a significant decrease in MDA levels. Metformin can protect cells and tissues against oxidative stress through inhibition of mitochondrial I complexes, preventing the production of mitochondrial ATP then there will be a transfer of the adenylate kinase reaction thus this change activates AMPK (Listyarini et al., 2021). Activation of AMP-activated protein kinase (AMPK) which reduces the activity of the enzyme acetyl CoA carboxylase (ACC) (Diniz Vilela et al., 2016).

Chia seeds of plants that contain antioxidants are quite high, their components consist of vitamin C, vitamin E, carotenoids, phenolic compounds, and polyphenolics which can be flavonoids (Baynes & Dominiczak, 2015). The flavonoid group that has antioxidant activity includes flavones, flavonols, isoflavones, catechins, flavonols, and calcon, micronutrients contained in plants such as vitamins A, C, E, folic acid, carotenoids, anthocyanins, and polyphenols have the ability to capture free radicals so that they can be used as a substitute for consumption of synthetic antioxidants (Gil et al., 2002). In a previous study conducted by Diyah, et al it was found that there was no meaningful relationship between plasma glucose levels related to renal MDA levels in the group of STZ-induced male rats who were given regular and measurable physical exercise or those who were not (Abad et al., 2017).

Consumption of chia seeds is associated with redistribution of lipids by recruitment of FAT/CD36 to the plasma membrane, mitochondrial activation and beta-oxidation (Nugroho et al., 2022). Lipid redistribution will improve glucose tolerance, this is related to reduced body adiposity because of its relation to ALA intake (Nasrulloh et al., 2021). ALA is an activator of AMPK, activation of AMPK will reduce blood glucose levels by phosphorylating AS160 protein which is a protein that plays a role in glucose transporters, increasing glucose uptake in an insulin independent pathway (Salafi et al., 2022). Chia seeds themselves can increase AMPK expression in the liver, so that AMPK can increase glucose absorption and oxidation, as well as glycolytic enzymes, resulting in increased glucose tolerance (Enes et al., 2020). Research conducted by Fonte-Feria, et al (2019) in mice fed the HFD diet showed the results that chia seeds could restore glucose and insulin tolerance. In a study conducted by (Vuksan, 2016) stated that chia seeds can maintain good glycemic and lipid control in well-controlled type 2 diabetes.

The authors hope that chia seeds can be an alternative for the treatment of diabetes mellitus but clinical trials must be carried out first

The limitations of this study lie in the incompleteness of organ histopathological examinations in wistar rats after the administration of chia seed extract in STZ-induced mice, and this study did not measure fasting blood sugar levels,

HbA1c levels.

Conclusions

Administration of chia seed extract doses of 4.5 mg/kgBB and 13.5 mg/kgBB can significantly reduce blood sugar levels during and MDA levels in male rats of the STZ-induced wistar strain.

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Conflict of interest

All authors know of no conflict 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, Syafinda Meisari Trisnani confirmed that the manuscript has been read and approved for submission by all the named authors.

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