The Effect of Aloe Vera Juice (*Aloe Vera*) on Blood Glucose Levels of Female White Rats (*Rattus Norvegicus*) Streptozotocin Induced Hyperglycemic

Delfi Ramadhini(✉) and Nefonafratilova Ritonga

University of Aufa Royhan, Padang Sidempuan City, Indonesia
delfiramadhini@gmail.com

Abstract. Diabetes Mellitus is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body cannot use the insulin it produces effectively. This condition results in an increase in glucose in the blood. Aloe vera contains chemicals that have hypoglycemic properties. This study aims to determine the effect of aloe vera juice on blood glucose levels of female white rats (Rattus norvegicus) induced by streptozotocin hyperglycemia. This study used a post test only control group design. The number of samples was 30 rats with a body weight of 150–200 mg and 2–3 months of age. Rats were divided into three groups, namely the negative control group, the positive control group and the treatment group. The dose of streptozotocin is 120mg/kgBW and aloe vera dose is 1.8 ml/200 gBW. Blood glucose measurements were carried out using a glucose meter. Data were analyzed by ANOVA test. The mean blood glucose level of the negative control rats was 60.70 ± 3.65 mg/dl, the positive control was 498.60 ± 89.77 mg/dl and the treatment was 77.4 ± 8.89 mg/dl. The results of the ANOVA test and post hoc test analysis showed that there was a significant difference in the average blood glucose levels in each group ($\rho < 0.05$). Aloe vera juice (Aloe vera) has an effect on reducing blood glucose levels of female white rats (Rattus norvegicus) with streptozotocin-induced hyperglycemia.

Keywords: aloe vera juice · blood glucose level · hyperglycemia

1 Introduction

According to the World Health Organization (WHO) (2016), diabetes mellitus (DM) is a serious and chronic disease that occurs when the pancreas does not produce enough insulin (a hormone that regulates blood sugar or glucose) or when the body cannot use the insulin it produces effectively. This condition results in an increase in glucose in the blood (Kemenkes 2014). Meanwhile, according to the American Diabetes Association (ADA) (2014), DM is a chronic and complex disease that requires continuous medical care to reduce the risk of getting out of control.

The incidence of DM has increased from year to year. In 1990 the number of DM in the world reached 80 million, in 1994 it increased to 110.4 million, and by 2010 it

S. H. Ritonga et al. (Eds.): TIHC 2022, AHSR 50, pp. 38–45, 2023.
https://doi.org/10.2991/978-94-6463-032-9_7

increased to 239.3 million (Arisman 2010; Sudoyo et al. 2007). According to WHO data (2016), diabetes caused 1.5 million deaths in 2012, and in 2014 as many as 422 million people in the world suffered from diabetes. In Southeast Asia the prevalence of DM increased from 4% in 1980 to 9% in 2014 (WHO 2016). In developed countries, more than 90% of DM cases are classified as type 2 DM. While in developing countries, 40% of DM sufferers are associated with community groups who change their lifestyle. This lifestyle change is in the form of a change in the traditional diet to a western diet which contains a lot of fat, sugar, salt and little fiber. In addition, changes in lifestyle from traditional to modern with the use of electronic devices that are completely instantaneous so that physical activity is less and does not exercise (Arisman 2010).

Indonesia is one of the 10 countries with the highest number of diabetes after India, China, the United States, the Russian Federation, Japan and Brazil. In 1995, Indonesia was ranked 7th, namely 4.5 million people and in 2025 it is predicted to increase to 5th rank with 12.4 million people (Sudoyo et al. 2007). According to data from the Ministry of Health (Kemenkes) in 2007, in Indonesia the prevalence of DM was 1.1%, while in 2013 the prevalence of DM was 2.1%. This figure shows that the incidence of DM has increased by 1%. Meanwhile, in 2013 based on gender, women had the highest percentage compared to men, namely 2.3% for women and 2.0% for men (Ministry of Health 2013).

DM disease can be divided into two, namely type 1 diabetes and type 2 diabetes. In type 1 diabetes, severe pancreatic damage occurs so that the body does not produce insulin or it is produced very minimally. Whereas in type 2 diabetes, insulin deficiency and insulin resistance can occur (Widowati 2008). Insulin resistance is a metabolic response disorder to insulin action, so that insulin levels are needed more than normal to achieve normal blood glucose levels (KGD). Both types of DM play a role in causing hyperglycemia conditions (Merentek 2006). According to WHO (2016) a hyperglycemic condition is when the glucose level in plasma is 7.0 mmol/L (126 mg/dL), with glucose levels of 110 and 126 mg/dL (6.1 to 7.0 mmol/L) is said to be a glucose tolerance state.

DM patients must control blood sugar, one of which is by taking hypoglycemic drugs. Chemical drugs tend to have side effects for their users. Therefore, it is necessary to conduct research using plants that have hypoglycemic properties, such as aloe vera.

Aloe vera contains chemicals that have hypoglycemic properties. Aloe vera contains vitamin A, vitamin C and vitamin E and contains minerals such as magnesium, copper, manganese, zinc, selenium, and iron. In addition, Aloe vera also contains 17 amino acids (Arifin 2015). Vitamins A, C and vitamin E contained in aloe vera function in reducing blood glucose, reducing oxidative stress by reducing ROS by terminating the lipid peroxide chain reaction thereby reducing MDA production, increasing antioxidant enzyme activity, and preventing complications (Mustofa 2015; Soviana et al. 2014, Yasin et al. 2015).

Research Mustofa et al. (2012) administration of aloe vera juice at a dose of 1.5 ml/head or 0.09 g/200gBW (450 mg/kgBW) can reduce blood glucose in hyperglycemic white rats. Another study by Rajasekaran et al. (2005), giving aloe vera extract at 0.06 g/200gBW (300 mg/kgBW) can reduce the KGD of diabetic rats. Research by Lestari et al. (2013) stated that giving 50 g of aloe vera decoction can reduce KGD in mice.

In some studies, the induction of streptozotocin (STZ) in rats can cause hyperglycemia in rats. The provision of antioxidants contained in aloe vera is expected to reduce KGD and reduce the effects of oxidative stress caused by hyperglycemic conditions. This condition can be seen from the decrease in blood glucose levels. Therefore, based on this problem, the researcher wanted to know the effect of giving aloe vera juice on the blood glucose levels of female white rats (Rattus norvegicus) induced by streptozotocin hyperglycemia.

2 Method

This type of research is an experiment using a post test only control group design. This research was conducted in December 2016 - October 2017 at the Laboratory of the Faculty of Pharmacy and the Laboratory of Biochemistry, Faculty of Medicine, Andalas University. The samples used were 30 female rats, 2–3 months old and weighing 150–200 gr which were divided into 3 groups. The KN group was only given standard feed, KP was induced by streptozotocin intraperitoneally at a dose of 20 mg/kg BW but was not given aloe vera juice and P was induced by steptozotocin intraperitoneally at a dose of 20 mg/kg BW and was given aloe vera juice orally at a dose of 1,8 ml/200 gBW/day.

For the KP and P groups, after 96 h of STZ induction, a KGD examination was carried out and if the rat's blood glucose was > 125 mg/dl, group III was given aloe vera juice at a dose of 1.8 ml/200 gBW/day orally for 12 days.

The rat's blood collection was carried out when the rat's body weight tended to increase and was stable in the KN group, KP group and P group. The rat's blood collection for checking blood glucose levels came from the tail end of the rat (lateral vein). Blood glucose measurements were carried out using a glucose meter (Gluco-DR).

This research has received ethical approval from the Research Ethics Committee at the Faculty of Medicine, Andalas University.

In this study, the data obtained were tested for normality of the data using the Shapiro Wilks test. If the data is normally distributed, then the ANOVA test is carried out with the level of confidence used is 95% ($\rho < 0.05$). If a significant result is obtained, it is continued with a statistical test (Multiple Comparison) Post Hoc Test with Bonferroni type to compare between groups.

3 Results

Based on Table 1 shows that blood glucose levels in each study group were normally distributed ($\rho > 0.05$). So that the next data processing is carried out by using the ANOVA parametric statistical test.

Based on Table 2, the mean difference in blood glucose levels (KGD) in the negative control group was 60.70 ± 3.65 mg/dl, an increase in the positive control group was 498.60 ± 89.77 mg/dl and there was another decrease in the positive control group. Treatment was 77.4 ± 8.89 mg/dl. The analysis of significance using the ANOVA test showed that statistically the difference in the mean KGD blood was significant ($\rho < 0.05$). So it was continued with a post hoc test with the Bonferroni type of test.

Table 1. Normality Test of Blood Glucose Levels in Each Research Group

No	Group	n	ρ	Information
1	KN	10	0,356	normal
2	KP	10	0,143	normal
3	P	10	0,935	normal

Table 2. Differences in Mean Blood Glucose Levels

No	Group	n	Blood Glucose Levels (mg/dl)	ρ
			Average ± SD	
1	KN	10	60,70 ± 3,65	0,000
2	KP	10	498,60 ± 89,77	
3	P	10	77,4 ± 8,89	

Table 3. Bonferroni Test Results of Blood Glucose Levels in Each Research Group

No	Group	KN	KP	P
1	KN		0,000*	1,000
2	KP			0,000*
3	P			

Table 4. Normality Test of Body Weight in Each Research Group

No	Group	n	ρ	Information
1	KN	10	0,246	normal
2	KP	10	0,232	normal
3	P	10	0,251	normal

The results of the Bonferroni test in Table 3 can be seen that blood glucose levels in the negative control group with the positive control group showed a significant difference ($\rho = 0.000$) and the positive control group with the treatment group showed a significant difference ($\rho = 0.000$).

Based on Table 4 shows that the body weight in each study group was normally distributed ($\rho > 0.05$). So that the next data processing is carried out by using the ANOVA parametric statistical test.

Table 5. Differences in Average Body Weight

No	Group	n	Body Weight (grams)	ρ
			Average ± SD	
1	KN	10	201,90 ± 10,66	0,000
2	KP	10	150,30 ± 10,41	
3	P	10	167,4 ± 13,37	

Table 6. Bonferroni Test Results on Body Weight in Each Research Group

No	Group	KN	KP	P
1	KN		0,000*	0,000*
2	KP			0,008*
3	P			

Based on Table 5, the difference in average body weight (BB) in the negative control group was 201.90 ± 10.66 g, there was a decrease in the positive control group, which was 150.30 ± 10.41 g and there was another increase in the treatment group, namely 167.4 ± 13.37 g. The analysis of significance using the ANOVA test showed that statistically the difference in the mean weight was significant ($\rho < 0.05$). So it was continued with a post hoc test with the Bonferroni type of test.

The results of the Bonferroni test in Table 6 can be seen that the weight of the negative control group with the positive control group showed a significant difference ($\rho = 0.000$), the negative control group and the treatment group showed a significant difference ($\rho = 0.000$) and the positive control group with the treatment group. Treatment showed a significant difference ($\rho = 0.008$).

4 Discussion

4.1 Effect of Aloe Vera (Aloe Vera) Juice on Blood Glucose Levels of Female White Rats (Rattus Norvegicus) Hyperglycemia

Streptozotocin is one of the diabetogenic substances that can induce hyperglycemia in rats. In this study it can be seen that the administration of STZ can cause hyperglycemic conditions. Hyperglycemic conditions in rats were characterized by an increase in blood glucose levels as shown in Table 2, the difference in the average blood glucose levels of each study group. The negative control rats resulted in normal blood glucose levels, namely 60.7 mg/dl and in the positive control rats it increased to 498.6 mg/dl.

Research related to the effect of streptozotocin on increasing blood glucose levels is a study by Fitri et al. (2016) intraperitoneal induction of streptozotocin at 180 mg/kgBW for three days can cause hyperglycemia in mice. Research by Krisnawati (2012), induction of streptozotocin at a dose of 150 mg/kgBW for two days can cause an increase

in blood glucose levels in rats. Meanwhile, according to research by Nugroho (2006) giving 100 mg/kgBW to rats can cause disturbances in the response to glucose and the sensitivity of cells to glucose. However, in this study, a dose of 120 mg/kgBW was used because streptozotocin induction at a dose of 180 mg/kgBW and 150 mg/kgBW could cause death in rats and a dose of 100 mg/kgBW could not cause hyperglycemia in rats.

Several theories explain that streptozotocin affects blood glucose levels. Streptozotocin is a toxic substance and is diabetogenic. Direct damage to pancreatic cells by streptozotocin can be seen from streptozotocin causing alkylation of pancreatic cell DNA through nutrourea groups. When streptozotocin is metabolized in cells, it will produce NO (nitric oxide), therefore stz becomes a NO (nitric oxide) donor thereby increasing the activity of guanyyl cyclase and the formation of cGMP. In addition, stz also inhibits the krebs cycle and reduces mitochondrial oxygen consumption so that the production of mitochondrial ATP is limited which then results in a drastic reduction in pancreatic cell nucleotides due to. As a result of limited ATP production, there is an increase in ATP dephosphorylation which will stimulate an increase in substrate for the xanthine oxidase enzyme and increase uric acid production. This xanthine oxidase enzyme can catalyze the formation of an active superoxide anion to form reactive oxygen species (hydrogen peroxide and superoxide radicals). Therefore, nitric oxide and reactive oxygen species formed from streptozotocin metabolism are the main causes of pancreatic cell damage, causing hyperglycemia conditions (Nugroho 2006).

Hyperglycemia also has an impact on weight loss of rats as shown in Table 5 the difference in the average weight of each study group. The negative control rats' average body weight was 201.9 g and in the positive control rats it decreased to 150.3 g.

Several theories explain that the use of diabetogenic substances can lose weight, examples of diabetogenic substances are streptozotocin and alloxan. Streptozotocin and alloxan are diabetogenic substances that can induce hyperglycemia in rats. A related study by Sweet et al. (2008) suggested that streptozotocin-induced diabetic rats experienced rapid weight loss and weight loss occurred between 4–10 days after induction. Winarsi research et al. (2013) stated that alloxan-induced rats with diabetes mellitus with glucose levels $>$ 200 mg/dl decreased their body weight.

Streptozotocin which can induce hyperglycemia rats can damage the pancreas, so that the function of the pancreas in producing the hormone insulin is disrupted. The hormone insulin is needed to regulate carbohydrate metabolism which will produce energy. The hormone insulin functions to help glucose in the blood enter the cells. If insulin production is disturbed, the cells will experience a lack of glucose and glucose cannot be metabolized into energy. Energy is something that the body must have, so the body will look for alternatives to produce that energy. The method used by the body is to overhaul fat stores in adipose tissue. Fat is hydrolyzed to produce fatty acids and glycerol. The continuous breakdown of fatty acids can result in the accumulation of acetoacetic acid in the body and can lead to the formation of ketone bodies (ketosis). Ketone bodies can be detected in urine and bad breath like ketones. In addition, the unavailability of glucose in the cells also results in excessive gluconeogenesis. Liver cells will increase the production of glucose from other substrates, one of which is by breaking down proteins. Amino acids resulting from the reshuffle are transcribed to produce substrates or intermediates in the formation of glucose. This event will take

place continuously because the insulin that limits the occurrence of gluconeogenesis is very little or even absent. As a result, there is a significant reduction in the amount of adipose tissue and muscle tissue. Thus, rats experiencing hyperglycemic conditions will experience severe body weight loss due to pancreatic damage (Murray et al. 2009; Suarsana et al. 2010; Winarsi et al. 2013).

5 Conclusions

Aloe vera juice (Aloe vera) has an effect on reducing blood glucose levels of female white rats (Rattus norvegicus) with streptozotocin-induced hyperglycemia. Aloe vera juice (Aloe vera) affects the weight gain of female white rats (Rattus norvegicus) induced by streptozotocin hyperglycemia.

References

Arifin, J. 2015. *Intensif Budidaya Lidah Buaya.* Yogyakarta: Pustaka Baru Press.

Arisman. 2010. *Obesitas, Diabetes Melitus dan Dislipidemia.* Jakarta: Penerbit Buku Kedokteran EGC.

[ADA] American Diabetes Association. 2014. "Standards of Medical Care in Diabetes". Diabetes Journals 37 (1)(14–80).

Fitri, S. R., Herla Rusmarilin, Ridwansyah. 2016. "Pengaruh Pemberian Polisakarida Larut Air Bengkuang (*Pachyrhizus erosus* L.) terhadap Mencit Penderita Diabetes Melitus". Jurnal Rekayasa Pangan dan Pertanian 4 (3): 360–370.

Krisnawati, D. E. 2012. "Efek Hipogykemia Pemberian Ekstrak Daun Johar pada Tikus (*Mus Musculus*) yang Diinduksi Streptozotosin". Jurnal Ilmu Kesehatan 1 (1): 59–63.

[Kemenkes] Kementerian Kesehatan Republik Indonesia. 2013. *Riset Kesehatan Dasar 2013.* Jakarta: Badan Penelitian dan Pengembangan Kesehatan.

[Kemenkes] Kementrian Kesehatan Republik Indonesia. 2014. *Situasi dan Analisis Diabetes.* Jakarta: Pusat Data dan Informasi.

Lestari, P. N., Tjandrakirana, Nur Kuswanti. 2013. "Pengaruh Pemberian Campuran Cairan Rebusan Kayu Secang (*Caessalpia sappan L.*) dan Daun Lidah Buaya (*Aloe vera*) terhadap Kadar Glukosa Darah Mencit (*Mus musculus*)". Jurnal Lentera Biologi 2 (1): 113–119.

Merentek, E. 2006. "Resistensi Insulin pada Diabetes Melitus Tipe 2". Jurnal Dunia Kedokteran 150: 38–41.

Murray, R. K., Daryl K. Granner, Victor W. Rodwell. 2009. *Biokimia Harper*. JakartaL EGC.

Mustofa, Ari Yuniastuti, Aditya Mariani. 2012. "Efek Pemberian Jus Lidah Buaya Terhadap Kadar Glukosa Darah Tikus Putih". Unnes Journal of Life Science 1 (1): 35–40.

Nugroho, A. E. 2006. "Review Hewan Percobaan Diabetes Melitus: Patologi dan Mekanisme Aksi Diabetogenik". Jurnal Biodiversitas 7 (4): 378–382.

Rajasekaran, S., Karuran Sivagnanam, Sotimuthu Subramanian. 2005. "Antioxidant Effect of Aloe vera Gel Extract in Streptozotocin Induced Diabetes in Rats". Pharmacological Reports 57: 90–96.

Soviana, Elida, Banundari Rachmawati, Nyoman Suci W. 2014. "Pengatuh Beta-karoten Terhadap Kadar glukosa Darah dan Kadar Malondialdehida pada Tikus *Sprague dawley* yang Diinduksi *Streptozotocin*". Jurnal Gizi Indonesia 2 (2): 41–46.

Suarsana, I. N., Bambang Pontjo Priosoeryanto, Tutik Wresdiyati, Maria Bintang. 2010. "Sintesis Glikogen Hari dan Otot pada Tikus Diabetes yang Diberi Ekstrak Tempe". Jurnal Veteriner 11 (3): 190–195.

Sudoyo, A. W., Bambang Setiyohadi, Idrus Alwi, Marcellus Simadibrata K dan Siti Setiati. 2007. *Ilmu Penyakit Dalam.* Jakarta: Pusat Penerbitan Departemen Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Indonesia.

Sweet, Ian R., Ofer Yanay, Lanaya Waldron, Merle Gilbert, Jessica M Fuller, Terry Tupling, Ake Lernmark, William R A Osborneb. 2008. "Treatment of Diabetic Rats With Encapsulated Islets". Journal of Cellular and Molecular Medicine 12 (6b): 2644–2650.

[WHO] World Health Organization. 2016. *Global Report on Diabetes.* Frence: WHO Library Cataloguing in Publication Date.

Widowati, W. 2008. "Potensi Antioksidan sebagai Antidiabetes". Jurnal Kesehatan Masyarakat 7 (2): 1–11.

Winarsi, H., Nurtjahjo Dwi Sasongko, Agus Purwanto, Indah Nuraeni. 2013. "Ekstrak Daun Kapulaga Menurunkan Indeks Atherogenik dan Kadar Darah Tikus Diabetes Induksi Aloksan". Jurnal Agritech 33 (3): 273–280.

Yasin, Yade Kurnia., Martha I Kartasurya, RA Kisdjimiatun. 2015. "Pengaruh Kombinasi Vitamin C dan vitamin E terhadap Kadar Malondialdehida Plasma Pasien Diabetes Melitus Tipe 2". Jurnal Gizi Indonesia 4 (1): 1–8.