FARMASAINS: JURNAL FARMASI DAN ILMU KESEHATAN
Volume 9, Number 2, 2024. p-ISSN: 2086-3373 I e-ISSN: 2620-987X
https://ejournal.umm.ac.id/index.php/farmasains

Research Article

Antidiabetic activity test of infusion combination rosella flower (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) in male mice (*Mus musculus*) induced by alloxan

Rasid Chaerul[(1)], Yovita Mercya[(1)]*

(1) Department of Farmacy, Faculty of Vocational Studies, Santo Borromeus University , Padalarang, West Java, Indonesia, City

* Corresponding author's email: ymercya@gmail.com

ARTICLE INFO

Article History
Submitted Sebtember 7, 2024
Revised October 29, 2024
Accepted, November 18, 2024
Published, November 30, 2024

Keywords
alloxan
cinnamon bark
diabetes mellitus
roselle flowers

DOI:
10.22219/farmasains.v9i2.36232.

ABSTRACT

Diabetes Mellitus (DM) is a disorder of carbohydrate, lipid and protein metabolism which is characterized by increased blood glucose levels. The existence of DM as a public health problem is increasing globally. This experimental research was carried out to determine the activity of a combination of rosella flower infusion and cinnamon bark on blood glucose levels in male mice that had been induced by alloxan. After ensuring that the blood glucose level of the mice was >175 mg/dl, 4 groups were tested, namely test group 1 was given a single rosella flower infusion, test group 2 was given a single cinnamon bark infusion, test group 3 was given a combination of rosella flower infusion and stem bark cinnamon, and the control group were given aqua destillata. Based on the results of the Kruskal-Wallis non-parametric statistical test, it shows a value of p = 0.009 (p ≤ 0,05), which means there is a difference in the reduction in blood glucose levels between the test groups. Then, to determine the greatest decrease in glucose levels, a post-hoc test was carried out and the highest mean rank value was obtained (13.00) in the infusion group of the combination of rosella flowers and cinnamon bark, followed by the cinnamon bark infusion group (5.80), and the rosella flower infusion group (5.20).

1. Introduction

Diabetes Mellitus (DM) is a disorder of carbohydrate, lipid, and protein metabolism characterized by elevated blood glucose levels (Wells et al., 2015). The International Diabetes Federation (IDF) in 2021

Cite: Rasid Chaerul (2024). Antidiabetic activity test of infusion combination rosella flower (Hibiscus sabdariffa L.) and cinnamon bark (Cinnamomum burmannii (Nees & T. Nees) Blume) in male mice (Mus musculus) induced by alloxan. Farmasains: Jurnal Farmasi dan Ilmu Kesehatan. 9 (2). 69-80. DOI : 10.22219/farmasains.v9i2.36232.

reported that 537 million people (aged 20-79 years) worldwide live with DM. This number is projected to increase to 643 million by 2030 and 783 million by 2045. In the 10th edition of the IDF Atlas, Indonesia ranked 5th with 19.47 million people affected, an increase of 81.8% compared to 2019, and this number is expected to reach 23.32 million by 2030 (International Diabetes Federation, 2021). The high prevalence of DM in Indonesia requires serious efforts to address this disease, one of which is through pharmacological therapy. DM pharmacological therapy can be carried out using Oral Hypoglycemic Agents (OHA) and insulin, or a combination of both. Based on previous studies, the use of OHA showed side effects such as nausea with metformin (18.25%) and glimepiride (13.33%), and hypoglycemia with glibenclamide (15.79%) (Joddy et al., n.d.). Due to these side effects, researchers continue to seek alternative natural-based drugs that can lower blood glucose levels, such as roselle flowers (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume).

The petals of roselle flowers (*Hibiscus sabdariffa* L.) contain chemical compounds such as gossypetin, anthocyanin, and hibisci glucosides, which in water solvent have antioxidant activity of 54.1%, thereby inhibiting free radicals in DM (Karmana, 2023; Mohd-Esa et al., 2010). Previous studies found that water extract of roselle petals has α-glucosidase enzyme inhibition activity of 82.6-93.5% (Urifah, 2011). By inhibiting the action of the α-glucosidase enzyme, it can delay the breakdown of oligosaccharides and disaccharides into monosaccharides (Shinde et al., 2008). According to previous research, roselle infusion significantly lowered blood glucose levels in mice at the 30th minute (Wahyuni and Sunoko, 2022).

Cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) contains chemical compounds such as Methylhydroxy Chalcone Polymer (MHCP), cinnamaldehyde, and proanthocyanidins (Emilda, 2018). Previous studies suggest that MHCP and cinnamaldehyde can enhance glucose transport through GLUT-4, thereby helping to lower blood glucose levels (Munthe, 2021; Ramadhan et al., 2023). Proanthocyanidin can prevent the formation of Advanced Glycation End Products (AGEs). The presence of AGEs triggers the formation of Reactive Oxygen Species (ROS), which can increase blood sugar production (Bernardo et al., 2015). Research conducted by Ahmad et al. in 2018 showed that the highest percentage of glucose-lowering effectiveness in mice occurred at the 60th minute after administering cinnamon bark infusion (Arrafi and Amanatie, 2018).

Roselle flowers (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) are expected to have synergistic benefits, but their activity as antidiabetic agents needs to be supported by scientific data. Research on the use of roselle flowers (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) individually as glucose-lowering agents has been conducted, but there has been no research on the effects of their combination. Additionally, one way of utilizing these plants is by making infusions, as the use of herbal plants in the community is often done by boiling. Based on this background, the researchers aim to investigate the activity of the combined infusion of roselle flowers (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) on blood glucose levels in male mice (*Mus musculus*) induced with alloxan.

2. Materials and Methods

This experimental study was conducted to determine the antidiabetic activity of a combination of roselle flower infusion (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) infusion, using a pretest-posttest control group design with 3 test groups and 1 negative control group. The pretest data represents the blood glucose levels of mice 72 hours after being induced with alloxan, while the posttest data represents the blood glucose levels of diabetic mice at the 60th minute after being given interventions, namely a single roselle flower (*Hibiscus sabdariffa* L.) infusion; a

single cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) infusion; a combination of roselle flower (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) infusion; and distilled water as the negative control.

The study was conducted in June 2024 at the Pharmacology Laboratory of Santo Borromeus University. The researchers have obtained the ethical clearance certificate for animal research issued by the Health Research Ethics Committee at the Faculty of Medicine, Maranatha Christian University, with decree No. 029/KEP/III/2024. The subjects used in this study were male mice (*Mus musculus*) obtained from breeders specifically for research purposes. The selection of mice was done using purposive sampling technique, with inclusion criteria of having a weight of 20-35 grams, being 2-3 months old, healthy and exhibiting normal activity, not previously used in other research studies, and having a blood glucose level >175 mg/dl after being induced with alloxan. The exclusion criteria in this study were male mice that died or became ill during the research. The World Health Organization (WHO) states that experimental studies should use at least 5 test animals, and therefore, 20 mice were required for this study since there are 4 treatment groups (Sugiyono, 2013; Ramadhan et al., 2023).

The tools used in this study include cages with food and water containers for the mice, Auto Check brand glucometer strips, an Auto Check glucometer, alcohol swabs, 1cc syringes and needles, thermometers, oral sondes, digital scales, beakers, and stirring rods. The materials used in this study include roselle flower simplicia, cinnamon bark simplicia, distilled water, 0.9% NaCl solution (500 mL), 5% sugar solution, and alloxan monohydrate.

Research Procedure

Preliminary Test

A preliminary test was conducted to ensure the success of the alloxan induction in the test animals. Three mice were fasted for 8 hours while still being given water, then induced with alloxan at a dose of 4 mg/20gBW intraperitoneally. After 5 hours of induction, the mice were given a 5% sugar solution for 24 hours to prevent hypoglycemia (Kumalasari et al., 2019). After 72 hours from the alloxan induction, blood glucose levels were checked to determine the effectiveness of alloxan in inducing diabetes.

Activity Test

The mice were acclimatized to the experimental environment for 7 days and maintained in the same manner. Before treatment, the test animals were fasted for 8 hours while still being given water to prevent dehydration. The mice were weighed to adjust the dose. The mice were randomly divided into 4 groups as follows, test group 1: Alloxan-induced group, then given roselle flower (*Hibiscus sabdariffa* L.) infusion; test group 2: Alloxan-induced group, then given cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) infusion; test group 3: Alloxan-induced group, then given a combination of roselle flower (*Hibiscus sabdariffa* L.) and cinnamon bark (*Cinnamomum burmannii* (Nees & T. Nees) Blume) infusion; and negative control group: Alloxan-induced group, then given distilled water.

Alloxan induction was carried out following the procedure described in the preliminary test flow. After 72 hours of alloxan induction, blood glucose levels were checked. Mice with blood glucose levels >175 mg/dl were used in the study (Noena et al., 2020). After 60 minutes of intervention, blood glucose levels were measured again in each test group. Blood samples for glucose measurement were taken intravenously from the mice's tails.

The negative control group, which was given distilled water, was used to ensure that the observed changes in blood glucose levels were due to the treatment with the test substances (roselle infusion,

cinnamon bark infusion, or their combination) and not due to other factors, such as external influences or normal physiological conditions. Additionally, the negative control also serves as a comparison to show that Alloxan induction successfully increased the blood glucose levels of the mice, providing a basis for testing the effects of the interventions. A positive control is typically required if there is a treatment or substance known to have a specific effect, such as an anti-diabetic drug that has been proven to lower blood glucose levels. However, in this study, the focus was on testing the potential of herbal substances (roselle and cinnamon) as alternative therapies, so a positive control was not necessary to achieve the objectives of this study (Huang et al., 2019).

Dose Determination and Preparation of Test Solutions

Alloxan Solution. Based on previous research, the dose of alloxan given was 200 mg/kgBW, so the dose for a 20-gram mouse was (20 g)/(1000 g) x 200 mg = 4 mg (Husna et al., 2019). The alloxan solution for a 20-gram mouse, with a volume of 0.2 mL, was administered intraperitoneally. Therefore, 200 mg of alloxan monohydrate was dissolved in 10 mL of 0.9% NaCl solution.

Roselle Flower Infusion (*Hibiscus sabdariffa* L.). According to previous research, the dose of roselle flower infusion given was 21 mg/20gBW (Wahyuni & Sunoko, 2022). The infusion for a 20-gram mouse was administered orally at 0.2 mL, so 10.5 grams of roselle flower was infused in 100 mL of distilled water.

Cinnamon Bark Infusion (*Cinnamomum burmannii* (Nees & T. Nees) Blume). Based on previous research, the dose of cinnamon bark infusion given was 1 g/kgBW, so the dose for a 20-gram mouse was (20 g)/(1000 g) x 1 g = 0.02 g or 20 mg (Arrafi and Amanatie, 2018). The infusion for a 20-gram mouse was administered orally at 0.2 mL, so 10 grams of cinnamon bark was infused in 100 mL of distilled water.

Combination Infusion. The combination infusion given was 21 mg/20gBW of roselle flower and 20 mg/20gBW of cinnamon bark. The infusion for a 20-gram mouse was administered orally at 0.2 mL. Therefore, 10.5 grams of roselle flower simplicia and 10 grams of cinnamon bark simplicia were infused in 100 mL of distilled water.

Data Processing and Analysis

Data processing was done by editing, selecting data based on inclusion and exclusion criteria, and entering the data into a table for processing. The processed data, displayed in tabular form, was statistically analyzed to determine the significance of differences between groups with a 95% confidence level. Hypothesis testing analysis was used to determine whether to accept or reject the null hypothesis (H0) and the alternative hypothesis (H1). If the p-value was ≤ 0.05, then there was a significant difference, and H0 was rejected. Since the data in this study was less than 30, non-parametric tests were used for hypothesis analysis.

Hypotheses 1, 2, and 3 were analyzed using the Wilcoxon test to determine whether there was a difference between pretest and posttest data in each test group (the single roselle flower infusion group, the single cinnamon bark infusion group, and the combination of roselle flower and cinnamon bark infusion group). Hypothesis 4 was analyzed using the Kruskal-Wallis test to determine whether there was a difference in the reduction of blood glucose levels in mice after intervention among the 3 test groups. If the result was significant, a post-hoc test was conducted to determine which group had the largest reduction in blood glucose levels after intervention at the 60th minute, based on the mean rank or average value determining the data ranking.

3. Results and Discussions

Preliminary Test

In this study, a preliminary test was conducted by injecting alloxan at a dose of 4 mg/20 g of mouse body weight (Husna et al., 2019). The preliminary test was conducted to observe the success of alloxan induction in damaging the pancreatic beta cells, which leads to an increase in the blood glucose levels of the mice. Blood samples were taken from the tail of the mice 72 hours after induction. The increase in blood glucose levels in the mice can be seen in **Table 1**. Based on the data in Table 1, it can be proven that alloxan induction successfully increased the blood glucose levels of the mice to above 175 mg/dl, making this dose suitable for use in this study.

Table 1. Increase in Blood Glucose Levels in the Preliminary Test

Object No.	Weight (g)	Alloxan Dose (mL)	Blood Glucose Level (mg/dl)
1	24,43	0,25	224
2	27,45	0,28	251
3	29,80	0,30	509

Activity Test

This study aims to evaluate the efficacy of various infusions in reducing blood glucose levels using 20 male mice induced with alloxan. The activity test measures blood glucose levels before and after intervention, as well as the reduction in blood glucose levels. Prior to treatment, the test animals were fasted for 8 hours, followed by alloxan induction according to the preliminary test procedure, and blood glucose levels were measured on the 3rd day (72 hours). After induction, Group 1 received a single infusion of roselle flower at 21 mg/20 g body weight of the mouse, Group 2 received a single infusion of cinnamon bark at 20 mg/20 g body weight of the mouse, Group 3 received a combination infusion of roselle flower (21 mg/20 g body weight) and cinnamon bark (20 mg/20 g body weight), while the negative control group received only distilled water. After 60 minutes of intervention, blood glucose levels were measured again from the tail of the mice. The average blood glucose levels before and after intervention for each group and the reduction in blood glucose levels can be seen in **Table 2**, and the comparison of blood glucose reduction is illustrated in **Figures 1 and Figure 2.**

Table 2. Average Blood Glucose Level in the Activity Test

Group	Average Blood Glucose Level (mg/dl)		Average Reduction in Blood Glucose Level (mg/dl) *)	Percentage Average Reduction in Blood Glucose Level (%) **)
	Pretest (P1)	Posttest (P2)		
Test 1	363, 4 ± 178,24	322,2 ± 165,39	41,2 ± 16,87	11,38
Test 2	187,2 ± 6,38	148,6 ± 13,16	38,6 ± 8,44	20,62
Test 3	401,2 ± 174,28	300,8 ± 170,64	100,4 ± 9,96	25,02
Negative Control	349,6 ± 121,96	396,2 ± 121,14	-46,6 ± 30,98	-13,33

Note:

*) The average reduction in blood glucose level is obtained from the difference between the average pretest and posttest blood glucose levels.

**) The percentage average reduction in blood glucose level is calculated using the formula:

$$\% \text{ Reduction} = \frac{P1-P2}{P1} \times 100\%$$

P1 = Average Blood Glucose Level Pretest P2 = Average Blood Glucose Level Posttest

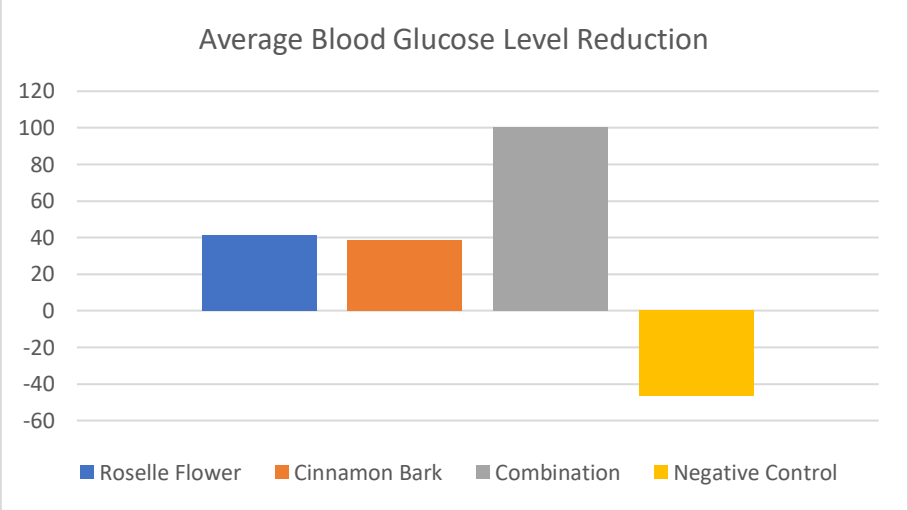

Figure 1. Diagram of Average Blood Glucose Level Reduction

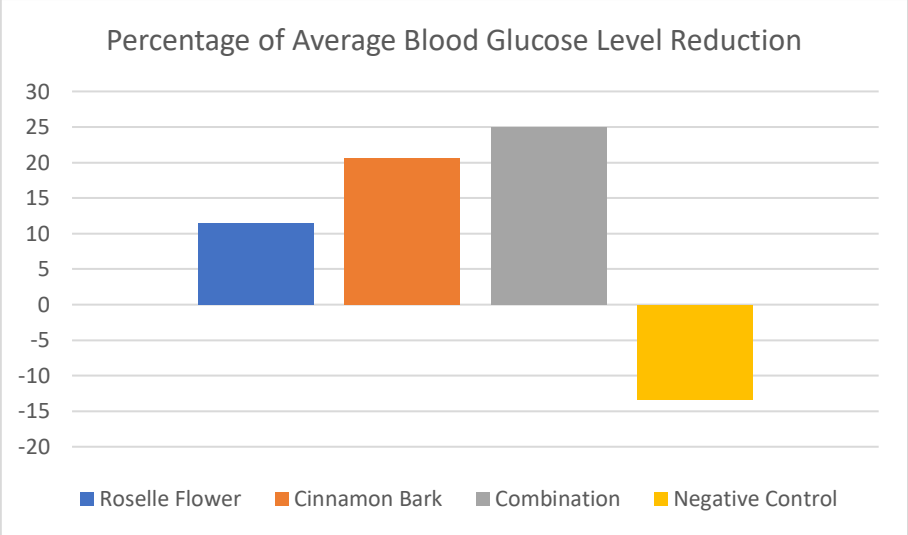

Figure 2. Diagram of Percentage of Average Blood Glucose Level Reduction

Antidiabetic Activity of Roselle Flowers

Based on the data in **Table 2**, it can be seen that administering roselle flower infusion reduced blood glucose levels by 11.38%. The antidiabetic activity of roselle flowers may be attributed to several chemical compounds present in them, such as gossypetin, anthocyanin, and hibiscus glucosides (Karmana, 2023). These three compounds act as antioxidants, which can help treat degenerative diseases such as diabetes mellitus (DM). Antioxidants are molecules that react with free radicals and neutralize them. Excessive oxidation reactions in the body can lead to the formation of highly reactive free radicals that can damage the structure and function of cells. In addition to being an antioxidant, previous research has shown that water extracts from roselle flowers inhibit the α-glucosidase enzyme (Mohd-Esa et al., 2010; Urifah, 2011). By inhibiting the activity of the α-glucosidase enzyme, the breakdown of oligosaccharides and disaccharides into monosaccharides is delayed (Shinde et al., 2008).

Antidiabetic Activity of Cinnamon Bark

Based on the data in **Table 2**, it can be seen that administering cinnamon bark infusion reduced blood glucose levels by 20.62%. The antidiabetic activity of cinnamon bark may be attributed to several chemical compounds present in it, such as Methylhydroxy Chalcone Polymer (MHCP), cinnamaldehyde, and proanthocyanidin. MHCP's mechanism of action involves increasing the concentration of IRS-1, an insulin receptor that activates the PI-3K pathway. This pathway promotes the synthesis of lipids, proteins, and glycogen through glycogen synthase and stimulates cell proliferation, supporting glucose distribution into cells. PI-3K then relocates GLUT-4 from the cytosol to the cell membrane, allowing glucose to enter the cell and be converted into ATP in the mitochondria. Cinnamaldehyde also increases glucose transport by GLUT-4 in adipose tissue and skeletal muscle. Additionally, cinnamaldehyde inhibits the α-glucosidase enzyme. Proanthocyanidin acts as an antioxidant by preventing the formation of Advanced Glycation End Products (AGE), which can trigger the formation of Reactive Oxygen Species (ROS), ultimately increasing blood sugar levels (Emilda, 2018; Munthe, 2021; Ramadhan et al., 2023; Bernardo et al., 2015).

Antidiabetic Activity of the Combination of Roselle Flowers and Cinnamon

Based on the data in **Table 2**, it can be seen that the combination of roselle flower and cinnamon bark infusion exhibited the greatest antidiabetic activity, reducing blood glucose levels by 25.02%. This suggests that the combination has a synergistic effect, utilizing different biological pathways to lower blood glucose levels, resulting in the most significant reduction. However, further research is needed to validate these findings, particularly concerning side effects and the effective dosage of the combination.

Hypothesis Testing

Differences in Blood Glucose Levels Before and After Treatment in Each Group

Hypotheses 1-3 were analyzed using the Wilcoxon test to assess the significance of differences in blood glucose levels before and after the administration of the test infusions at 60 minutes.

- The result of Hypothesis 1 testing showed a p-value = 0.043 ($p \leq 0.05$), leading to the rejection of H0 and the acceptance of H1, indicating a significant difference in blood glucose levels before and after administering the single roselle flower infusion at 60 minutes
- The result of Hypothesis 2 testing showed a p-value = 0.043 ($p \leq 0.05$), leading to the rejection of H0 and the acceptance of H1, indicating a significant difference in blood glucose levels before and after administering the single cinnamon bark infusion at 60 minutes
- The result of Hypothesis 3 testing showed a p-value = 0.043 ($p \leq 0.05$), leading to the rejection of H0 and the acceptance of H1, indicating a significant difference in blood glucose levels before and after administering the combination of roselle flower and cinnamon bark infusions at 60 minutes

Differences in Blood Glucose Level Reductions Between Groups

Hypothesis 4 was analyzed using the Kruskal-Wallis test to determine the significance of differences in blood glucose level reductions after administering single roselle flower, single cinnamon bark, and combined roselle flower and cinnamon bark infusions at 60 minutes. The result of Hypothesis 4 testing showed a p-value = 0.009 ($p \leq 0.05$), leading to the rejection of H0 and the acceptance of H1, indicating a significant difference in blood glucose level reductions between the test groups. A post hoc test was then conducted to determine which group showed the greatest reduction in blood glucose levels. The post-hoc test results indicated that Group 3, which received the combination of roselle flower and cinnamon bark

Cite: Rasid Chaerul (2024). Antidiabetic activity test of infusion combination rosella flower (Hibiscus sabdariffa L.) and cinnamon bark (Cinnamomum burmannii (Nees & T. Nees) Blume) in male mice (Mus musculus) induced by alloxan. 9 (2). 81-89. DOI : 10.22219/farmasains.v9i2.36232.

infusions, had the largest reduction in blood glucose levels, with a mean rank of 13.00, followed by Group 2 and Group 1, with mean ranks of 5.80 and 5.20, respectively.

4. Conclusions

Based on the results of the study on the 4 treatment groups, the following conclusions were drawn:

1. The administration of single roselle flower infusion, single cinnamon bark infusion, and the combination of roselle flower and cinnamon bark infusion significantly affected blood glucose levels before and after treatment at the 60th minute
2. There was a difference in the reduction of blood glucose levels after administering single roselle flower infusion, single cinnamon bark infusion, and the combination of roselle flower and cinnamon bark infusion at the 60th minute, as evidenced statistically by a *p*-value of 0.009 ($p \leq 0.05$).
3. The combination of roselle flower infusion and cinnamon bark infusion resulted in the greatest reduction in blood glucose levels, with a mean rank value of 13.00.

5. References

Arrafi, A. N., & Amanatie. (2018). Uji aktivitas antidiabetes infusa kulit batang kayu manis (Cinnamomun burmanii) pada mencit putih jantan secara in vivo.

Bernardo, M. A., Silva, M. L., Santos, E., Moncada, M. M., Brito, J., Proença, L., Singh, J., & De Mesquita, M. F. (2015). Effect of Cinnamon Tea on Postprandial Glucose Concentration. *Journal of Diabetes Research*, *2015*. https://doi.org/10.1155/2015/913651

Emilda. (2018). EFEK SENYAWA BIOAKTIF KAYU MANIS Cinnamomum burmanii NEES EX.BL.) TERHADAP DIABETES MELITUS: KAJIAN PUSTAKA. In *Jurnal Fitofarmaka Indonesia* (Vol. 5, Issue 1). www.jurnal.farmasi.umi.ac.id/index.php/fitofarmakaindonesia

Huang, W., Percie du Sert, N., Vollert, J., & Rice, A. S. C. (2019). *General Principles of Preclinical Study Design* (pp. 55–69). https://doi.org/10.1007/164_2019_277

Husna, F., Suyatna, F. D., Arozal, W., & Purwaningsih, E. H. (2019). Model Hewan Coba pada Penelitian Diabetes Animal Model in Diabetes Research. *Mini Review Article Pharmaceutical Sciences and Research (PSR)*, *6*(3), 131–141.

International Diabetes Federation. (2021). *IDF Diabetes Atlas 10th Edition*.

Joddy, R., Putra, S., Achmad, A., & Rachma, H. (n.d.). Kejadian Efek Samping Potensial Terapi Obat Anti Diabetes Pasien Diabetes Melitus Berdasarkan Algoritma Naranjo. In *PHARMACEUTICAL JOURNAL OF INDONESIA* (Vol. 2017, Issue 2). http://.pji.ub.ac.id

Karmana, I. W. (2023). Artikel Review : Bioaktivitas Bunga Rosella (Hibiscus sabdariffa L.) Beserta Pemanfaatannya. *Educatoria : Jurnal Ilmiah Ilmu Pendidikan*, *3*(3), 208–216. https://doi.org/10.36312/educatoria.v3i3.200

Kumalasari, E., Susanto, Y., Yulia Rahmi, M., & Rizky Febrianty, D. (2019). PENGARUH PEMBERIAN EKSTRAK ETANOL DAUN RAMANIA (Bouea macrophylla Griffith) TERHADAP PENURUNAN KADAR GULA DARAH MENCIT PUTIH (Mus muscullus) YANG DIINDUKSI ALOKSAN. *JCPS (Journal of Current Pharmaceutical Sciences)*, *2*(2), 173–179.

Mohd-Esa, N., Hern, F. S., Ismail, A., & Yee, C. L. (2010). Antioxidant activity in different parts of roselle (Hibiscus sabdariffa L.) extracts and potential exploitation of the seeds. *Food Chemistry*, *122*(4), 1055–1060. https://doi.org/10.1016/j.foodchem.2010.03.074

Munthe, R. M. I. (2021). Potensi Kayu Manis sebagai Antidiabetik. *Jurnal Penelitian Perawat Profesional*, *3*(2), 303–310. https://doi.org/10.37287/jppp.v3i2.451

Noena, R. A, Thahir, Z., Hidayah Base, N., & Fahriani. (2020). AKTIVITAS ANTI HIPERGLIKEMIA MINYAK KLUWAK PADA HEWAN UJI MENCIT (Mus Musculus). *Journal Kesehatan Yamasi Makassar*, *4*(1), 40–46.

Ramadhan, M.G., Wahyu, S., Arfah, A. I., Makmun, A., & Murfat, Z. (2023). *Pengaruh Pemberian Ekstrak Kayu Manis (Cinnamomun burmanii) terhadap Penurunan Kadar Gula Darah pada Mencit (Mus musculus)*.

Shinde, J., Taldone, T., Barletta, M., Kunaparaju, N., Hu, B., Kumar, S., Placido, J., & Zito, S. W. (2008). α-Glucosidase inhibitory activity of Syzygium cumini (Linn.) Skeels seed kernel in vitro and in Goto–Kakizaki (GK) rats. *Carbohydrate Research*, *343*(7), 1278–1281. https://doi.org/10.1016/j.carres.2008.03.003

Sugiyono. (2013). *METODE PENELITIAN KUANTITATIF, KUALITATIF, DAN R&D* (I). Alfabeta.

Urifah, I. (2011). *DAYA INHIBISI EKSTRAK ROSELLA (Hibiscus sabdariffa) TERHADAP ENZIM ALFA-AMILASE, ALFA-GLUKOSIDASE DAN LIPASE SECARA IN VITRO*.

Wahyuni, D. U., & Sunoko, H. R. (2022). Pengaruh Pemberian Infusa Kelopak Bunga Rosella (Hibiscus sabdariffa L.) sebagai Penurun Kadar Glukosa Darah pada Mencit Putih Jantan (Mus Musculus Galur Swiss-Webster) yang Diinduksi Glukosa. *Generics: Journal of Research in Pharmacy*, *2*(1), 54–60. https://doi.org/10.14710/genres.v2i1.11269

Wells, B. G., DiPiro, J. T., Schwinghammer, T. L., & DiPiro, C. V. (2015). *Pharmacotherapy Handbook: Ninth Edition*.

Cite: Rasid Chaerul (2024). Antidiabetic activity test of infusion combination rosella flower (Hibiscus sabdariffa L.) and cinnamon bark (Cinnamomum burmannii (Nees & T. Nees) Blume) in male mice (Mus musculus) induced by alloxan. 9 (2). 81-89. DOI : 10.22219/farmasains.v9i2.36232.