



Antidiabetic Effect Test of Combination of Ginger (*Zingiber officinale*), Lemongrass (*Cymbopogon citratus*), and Cinnamon (*Cinnamomum verum*) on Male Mice (*Mus musculus*)

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Abstract. Diabetes mellitus (DM) or diabetes is a disease caused by disorders related to the hormone insulin. Ginger, lemongrass and cinnamon are traditional plants that have the potential to be developed as herbal medicines. The combination of these traditional plants can be used as an alternative treatment for diabetes mellitus. Infusions of ginger, lemongrass and cinnamon contain secondary metabolites, namely flavonoids, terpenoids and tannins. These three active compounds have antioxidant, antidiabetic, and anti-inflammatory activities. The aim of this study was to determine the antidiabetic effect of the infusion of a combination of JSKM (ginger (*Zingiber officinale*), lemongrass (*Cymbopogon citratus*) and cinnamon (*Cinnamomum verum*)) on male mice (*Mus Musculus*). The design of this research is experimental with data analysis method using SPSS 16.0. Observation of healing time is done by observing the decrease in blood sugar levels for 7 days. In this study, 5 treatment groups were used, namely the negative control group (aquadest), the positive control group (glibenclamide), the P1 dose (162 mg/kgBW), the P2 dose (324 mg/kgBW), and the P3 dose (486 mg/kgBW). The most effective dose of the antidiabetic effect of JSKM infusion in male mice was in the P3 group with a dose of 486 mg mg/kgBW.

Keywords: Antidiabetic · Stew · Ginger · Lemongrass · Cinnamon

1 Introduction

Diabetes mellitus (DM) or diabetes is a disease caused by disorders related to the hormone insulin. The abnormality in question is in the form of a reduced amount of insulin hormone production due to the inability of the pancreas to produce, or the body's cells cannot use the insulin it produces [1].

Antidiabetic is an activity given by certain compounds that can treat diabetes. Antidiabetic drugs that are often prescribed by doctors such as metformin, sulfonylureas, meglitinide, thiazolidinediones (glitazone), DPP-4 inhibitors (gliptin), GLP-1 receptor agonists (inkretin mimetics), SGLT2 inhibitors [1].

Bioactives from citronella plants such as flavonoids, tannins, saponins, polyphenols, alkaloids, and vitamins A, and C, have been recognized as antioxidants that tend to contribute to antidiabetic and lipid effects [2]. Ginger contains active ingredients such as alkaloids, flavonoids, and saponins. Ginger juice can reduce glucose levels in rats induced with Alloxan.^{ln}

Addition, cinnamon is known to have benefits in lowering glucose levels in a person's body. Not only ginger and lemongrass, there is also cinnamon which has been clinically proven to fight free radicals. Ervina stated that the extract of the bark of *Cinnamomum burmanii* contains the main antioxidant compounds in the form of polyphenols (tannins, flavonoids) and phenolic essential oils [3].

Utilization of several biological plant raw materials from leaves, flowers, seeds, roots and bark to make herbal drinks has been used for many years to treat various problems. Seeing from the activities and demands of work that is increasing, it is difficult for people to live a healthy lifestyle. In addition, the increasing number of diabetes mellitus causes concern in the hearts of the public to care about increasing the body's resistance [4].

Referring to the problems that have been presented in previous studies that there is no literature discussing the infusion of a combination of ginger, lemongrass, and cinnamon for antidiabetic treatment, the researchers were interested in taking the title “**Test of Antidiabetic Effects of Combination of Ginger (*Zingiber officinale*), Lemongrass (*Cymbopogon citratus*), Cinnamon (*Cinnamomum verum*) in Male Mice (*Mus Musculus*)**”. It is hoped that the discovery of this herbal combination drug can help treat diabetes mellitus.

2 Methods

The research design used is an experimental study in a laboratory that aims to find out what happens as a result of the antidiabetic effect of steeping a combination of ginger, lemongrass and cinnamon in mice. The type of data used is primary data obtained through direct examination of the decrease in blood glucose levels of mice (*Mus musculus*). The data collection technique in this study was carried out by checking the blood glucose levels of Pre-DM and DM mice (*Mus Musculus L.*).

The tools used were mouse cages, glass beakers, stirring rods, scales, syringes, POCT (*Auto Check*), glucose strips, hot plates. While the ingredients used were alloxan, ginger, lemongrass and cinnamon, glibenclamide, aquadest, male mice. This research was conducted at the Biology Laboratory of the Medica Farma Husada Mataram Polytechnic in February 2022. The population in this study was ginger, lemongrass and cinnamon. While the samples used in this study were steeping ginger, lemongrass and cinnamon. The number of replicated mice used in this study was 25 mice, which were divided into 5 groups. After that, 25 mice were divided into 5 treatment groups. The treatment groups included:

- Group 1:** As a negative control group (K-) was given aquadest for 7 days
- Group 2:** As a positive control group (K+) was given glibenclamide at a dose of 0.65 mg/kg BW for 7 days
- Group 3 (P1):** Treatment 1 was steeped in a combination of JSKM at a dose of 162 mg/kgBW for 7 days
- Group 4 (P2):** Treatment 2 was steeped in a combination JSKM at a dose of 324 mg mg/kgBW for 7 days
- Group 5 (P5):** Treatment 3 was steeped in a combination of JSKM with dose of 486 mg/kgBW for 7 days

After treatment, the mice were rested in their respective cages and given standard feed and aquadest as usual. On the 3rd day, blood samples were taken from all the test animals. Furthermore, after 4 days of treatment with blood sugar levels, the mice were measured their blood glucose levels up to day 7 to compare blood glucose levels after being given alloxan.

Furthermore, after the data is collected, computerized data processing is carried out using SPSS version 16.0. The first test conducted was the normality test using Shapiro-Wilk to determine whether the data was normally distributed or not. If the distribution is normal then it is continued with the One-Way Anova test and vice versa. If the data is not normally distributed then it is continued with the non-parametric test, namely the Kruskal Wallis test. The Tukey test was continued to determine the difference in each dose of the combination of ginger, lemongrass and cinnamon.

3 Results and Discussion

The results of blood sugar measurements of mice in the positive control group, negative control group, a dose of 162 mg/kg BW, a dose of 324 mg mg/kg BW, a dose of 486 mg/kg BW are shown in Fig. 1.

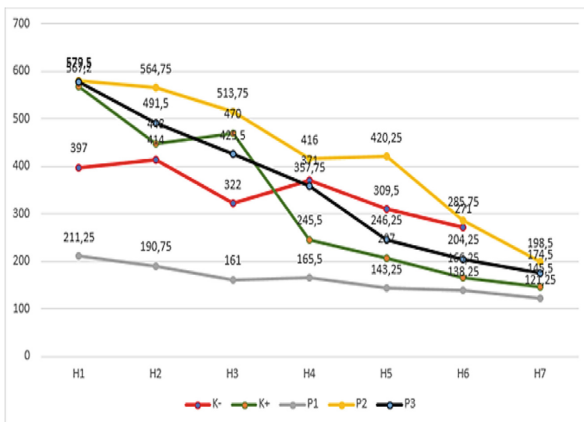


Fig. 1. Graph of Mice Blood Sugar Measurement.

Table 1. Normality Test Results Data using the Shapiro Wilk Test

Variable	Sig Shapiro Wilk	Z Table Value (5%)	Description
Antidiabetic Effect Test of Combination of Ginger, Lemongrass, and Cinnamon	0,005	0,05	H1 Accepted

Table 2. Results of Homogeneity Test using Levene's

Variable	Sig	Level (5%)	Description
Antidiabetic Effect Test of Combination of Ginger, Lemongrass, and Cinnamon	0,000	0,05	H1 Accepted

Table 3. Results of the Kruskal-Wallis Test of Antidiabetic Effects of Ginger, Lemongrass, and Cinnamon

Source	Sig	Description
Antidiabetic Effect Test of Combination of Ginger, Lemongrass, and Cinnamon	0,033	Rejected H0

Based on the Fig. 1, it can be seen that the administration of a combination of ginger, lemongrass and cinnamon infusion has an effect on decreasing blood glucose levels in mice. The highest blood glucose levels were found in group 5 (P3) with a dose of 486 mg/kgBW showing an average value of 425.5 mg/dL, the group with the lowest blood glucose levels was found in the negative or normal control group with an average value of 159 mg/dL.

The results of the normality test in groups I, II, III, IV, V in Table 1 can be seen that for the test data for the antidiabetic effect of steeping the combination of ginger, lemongrass, and cinnamon, the p_value of Shapiro Wilk smaller than the value of the significant level or 5% error. So it was decided that there was acceptance of H1, which means that the test data for the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon did not follow the normal distribution pattern.

While the homogeneity test based on Table 2. It can be seen that for the test data for the antidiabetic effect of steeping the combination of ginger, lemongrass, and cinnamon, the P_value (Sig) (0.055) is greater than the 5% significance level or 0.05. So it was decided that there was acceptance of H1, which means the test data for the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon infusion were not homogeneous. Because the data does not meet the normality and homogeneity assumption tests, the data can be continued for the analysis phase using the Kruskal-Wallis test.

Table 4. Tukey's Test Results of Antidiabetic Effects of Ginger, Lemongrass, and Cinnamon

Dosage	1	2	3
K- (Aquadest)	-157		
P1- (Dosage of 162 mg/kgBB)		192,5	
K+ (Glibenklamid dosage 0,65 mg/kgBB)			221
P2 (dosage 324 mg/kgBB)			392
P3 (Dosage 486 mg/kgBB)			425,5

Based on Table 3 it can be seen that the results of the Kruskal-Wallis test show the results of the hypothesis test that have been stated previously. The value in the column Sig. showed a significant value for the test data for the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon infusion. The significant value for the test data for the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon is 0.033 (smaller than the specified error, which is 5%). So the decision taken is to reject H_0 which means that there is a significant effect on the difference in the dose of the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon infusion on male mice.

The next test was carried out to find out which concentrations were different by using the Tukey test. Based on the results of SPSS analysis, it can be seen that for the difference in concentration on the test data for the antidiabetic effect of steeping the combination of ginger, lemongrass, and cinnamon, they were divided into 3 groups, namely the first group K- (Aquadest), the second group P1 (dose 162 mg/kgBW), and the second group P1 (dose of 162 mg/kgBW), and the three K+ (glibenclamide dose 0.65 mg/kg BW), P2 (dose 324 mg mg/kgBW) and P3 (486 mg mg/kgBW). The dose in 1 group was considered to have the same effect while between groups there was a significant difference (Table 4).

The K- (Aquadest) treatment had a different effect from other treatments. Likewise with the P1 treatment (dose of 162 mg/kgBW) which was also different from the other treatments. Meanwhile, K+ (glibenclamide dose 0.65 mg/kg BW), P2 (324 mg mg/kgBW) and P3 (486 mg mg/kgBW) were considered to have the same effect as antidiabetic. For the best dose of the test dose for the antidiabetic effect of steeping the combination of ginger, lemongrass, and cinnamon, namely at P3 with a dose of 486 mg mg/kgBW with the average difference with the positive control treatment K+ only 204.5.

Each *simplicia* ginger, lemongrass, and cinnamon has many benefits. The chemical compounds that are thought to play a role in the antidiabetic activity of the JSKM combination infusion are flavonoids. Flavonoids are compounds that can lower blood sugar levels, as inhibitors of the -glucosidase enzyme in reducing intestinal glucose and fructose absorption. The workings of flavonoid compounds have been shown to have beneficial effects in fighting diabetes, both through the ability to control blood sugar levels and optimize the work of the pancreas organ by increasing the sensitivity

of pancreatic beta cells. So that it can produce the hormone insulin which is needed to regulate blood glucose levels in the body.^{JSKM}.

Combination, such as terpenoids which have the same receptor function as sulfonylurea drugs, which will cause cells to release more insulin in a short time. The main mode of action of terpenoids is to increase insulin sensitivity. While tannins have a role to stimulate glucose transport by activating the insulin signaling pathway. The mechanism of action of tannins in reducing blood glucose levels is to reduce nutrient absorption by inhibiting glucose absorption in the intestine, besides inducing the regeneration of pancreatic cells which have an effect on adipose cells thereby strengthening insulin activity.

In previous studies, it was found that there was a significant decrease in blood glucose levels through the administration of ginger (*Zingiber officinale*) juice in the diabetic and non-diabetic groups. The antidiabetic activity of *Zingiber officinale* is related through 5-HT antagonism (6-gingerol chemical receptors and biological markers present in *Zingiber officinale*). The results showed a current 5-HT antagonist activity for the effects of methanol and its clusters in STZ-induced NIDDM rats. Research on ginger with its antioxidant properties is a study conducted on rats that were previously induced with STZ, where this STZ will reduce antioxidant levels, then by giving ginger diet it was found that antioxidant levels increased significantly.

Antioxidants function to reduce oxidative damage due to hyperglycemic conditions. Hyperglycemia is involved in the formation of free radicals. Increasing levels of antioxidants are sufficient to prevent clinical complications in DM, which include inhibiting microvascular complications, decreasing the incidence of coronary heart disease, improving the autonomic nervous system in the heart, and vasodilatation of blood vessels different antidiabetic activities. Among them, research by Tjahjani et al. [5] proved that giving a dose of 20.8 mg of cinnamon ethanol extract to mice was able to lower blood glucose. Cinnamon extract dose of 20.8 mg was as effective as glibenclamide in lowering blood glucose. Similarly, Alusinsing et al. [6] also proved a decrease in blood sugar levels in mice after being given ethanol extract of cinnamon bark.

Research by Kusumaningtyas et al. [7] by giving cinnamon powder steeping at a dose of 0.73 mg/g bw was able to improve the pancreatic structure of male mice with Balb-C Strain after being exposed to alloxan. The administration of lemongrass steeping at a dose of 3.6 ml/200grBB and 0.9 ml/200grBW rats showed that lemongrass stew was able to reduce blood glucose, triglyceride, LDL and total cholesterol levels, as well as increase HDL levels [4].

4 Conclusion

Based on the results of research on the antidiabetic effect of the infusion of ginger (*Zingiber officinale*), lemongrass (*Cymbopogon citratus*) and cinnamon (*Cinnamomum verum*) in male mice (*Mus Musculus*), it can be concluded that:

- 1) Based on the results of the Kruskal Wallis test, the significant value for the data on the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon infusion was 0.033 (smaller than the specified error, which was 5%). So it was decided that

there was a significant effect on the difference in the test dose of the antidiabetic effect of the combination of ginger, lemongrass, and cinnamon infusion on male mice.

- 2) Judging from the results of the Tukey test, the dose of the JSKM combination steeping that had the best antidiabetic effect in male mice was in the P3 group with a dose of 486 mg mg/kgBW.

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