RESEARCH ARTICLE

Antihyperglycemic Effect of Polyherbal Tea From Moringa oleifera, Cymbopogon citratus, and Stevia rebaudiana Leaves in Alloxan and HFD-Induced Mice (Mus musculus)

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ABSTRACT

Diabetes Mellitus (DM) is a disease with metabolic disorders characterized by chronic hyperglycemia and disorders of carbohydrate, fat, and protein metabolism due to insulin secretion disorders. In general, DM patients require pharmacotherapy such as injected insulin or oral antidiabetic drugs. Pharmacological treatment is relatively expensive and needs to consider its efficacy and safety. Therefore, this study explores natural sources such as medicinal plants. The aim of this study was to determine the antihyperglycemic effect of a combination of boiled moringa leaves, lemongrass leaves and stevia leaves on mice (Mus musculus) induced by alloxan. In this study, 25 mice were divided into 5 groups. The mice will undergo adaptation for 7 days and then given HFD for 30 days. After 30 days, the mice will be given alloxan 170 mg/kgBW for 3 days to induce DM. After DM was successfully induced in mice, polyherbal tea combination of moringa leaves, lemongrass leaves and stevia leaves was made and given, then continued with evaluation blood glucose, blood glucose percentage, body weight, body weight percentage, index lee and liver organ index. The group given herbal tea combination of moringa leaves (Moringa oleifera), lemongrass leaves (Cymbopogon citratus) and stevia leaves (Stevia rebaudiana) with a concentration of 3.6 mg/mL showed a better decrease in KGD and %KGD compared to other treatment groups. The decrease in BB, %BB and lee index was better in the group given a combination of Moringa leaves (Moringa oleifera), Lemongrass leaves (Cymbopogon citratus) and Stevia leaves (Stevia rebaudiana) with a concentration of 7.2 mg/mL. The decrease in the liver organ index was also better seen in the group given a combination of Moringa leaves (Moringa oleifera), Lemongrass leaves (Cymbopogon citratus) and Stevia leaves (Stevia rebaudiana) with a concentration of 7.2 mg/mL. The group given herbal tea combination of Moringa leaves (Moringa oleifera), Lemongrass leaves (Cymbopogon citratus) and Stevia leaves (Stevia rebaudiana) with a concentration of 3.6 mg/mL reduced BG and BG percentage, while the group given herbal tea combination of Moringa leaves (Moringa oleifera), Lemongrass leaves (Cymbopogon citratus) and Stevia leaves (Stevia rebaudiana) with a concentration of 7.2 mg/mL reduced BW, BW percentage, Lee index, and hait organ index.

Keywords: Diabetes, Moringa Leaves, Lemongrass Leaves, Stevia Leaves, Blood Glucose Levels, Body Weight

INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia and impaired carbohydrate, fat, and protein metabolism due to impaired insulin secretion. DM is long-term or chronic, characterized by increased blood glucose concentrations due to the body's inability to produce one or enough insulin, or its inability to effectively use the insulin it produces. There are four types of DM: type 1 DM (T1DM), type 2 DM (T2DM), maturity-onset diabetes of the young (MODY), and gestational diabetes (GDM) (1). Ninety percent of DM cases are type 2, characterized by decreased insulin sensitivity and/or insulin secretion. Genetic factors and environmental influences significantly contribute to type 2 DM. Other causes of type 2 DM include obesity, a high-fat, low-fiber diet, and lack of exercise (2).

Pharmacological treatment is relatively expensive and requires careful consideration of efficacy and safety, especially when using antidiabetic drugs, which are largely metabolized in the liver. The risk of side effects must also be monitored. One of the most frequently prescribed diabetes medications is metformin. Metformin is widely used as a first-line therapy for T2DM, but it has side effects (AEs), including gastrointestinal disturbances such as diarrhea, nausea, vomiting, and flatulence (11). Metformin is generally taken for a long period of time, which can increase the risk of side effects (12).

Moringa oleifera leaves, or Moringa, have antihyperglycemic activity by inhibiting the α-glucosidase enzyme found in the brush border of the small intestine. Moringa oleifera leaves also contain various polyphenols and flavonoids, including quercetin-3-glycoside (Q-3-G: 1494.2 μmol/100 g dry weight), rutin (1446.6 μmol/100 g dry weight), kaempferol glycoside (394.4 μmol/100 g dry weight), and chlorogenic acid (134.5 μmol/100 g dry weight). Of the polyphenols mentioned above, Q3G has a blood glucose-lowering effect. Q3G influences glucose intake in the small intestinal mucosa, prolonging glucose absorption into the bloodstream, ultimately lowering blood sugar levels (13).

The active compounds in the aqueous extract of Moringa oleifera leaves contribute to their antihyperglycemic properties: terpenoids, polyphenols, and quercetin. Terpenoids stimulate insulin secretion, thereby controlling blood glucose levels. Previous research, according to Manohar et al., demonstrated that Moringa oleifera leaves have antidiabetic activity, both in vivo and in vitro. reported an in vivo study on diabetic rats given Moringa leaf water extract at doses of 100, 200, and 300 mg/kg body weight, showing hypoglycemic activity of 14.03%, 15.2%, and 14.22%, respectively. (14)

Lemongrass is an herbal plant with chemical compounds consisting of secondary metabolites such as alkaloids, saponins, tannins, flavonoids, phenols, and steroids, which can act as antidiabetics. (15) This plant has various benefits, such as boosting immunity, reducing blood cholesterol, improving sleep quality, relieving pain. Processed lemongrass products can repel mosquitoes, freshen the air, and reduce stress. Two types of lemongrass generally grow in Indonesia: fragrant lemongrass (Cymbopogon sp.) and kitchen lemongrass (Cymbopogon citratus). The type of lemongrass used is kitchen lemongrass (Cymbopogon citratus). Lemongrass also acts as an aromatizer and can help diabetics

enjoy herbal tea combinations with a calming aroma. (16)

The addition of stevia to boiled moringa leaves and lemongrass leaves in herbal tea for type 2 DM sufferers is a safe sweetener, especially in the management of insulin sensitivity and type 2 DM. (17) Based on the content of moringa leaves (Moringa oleifera) and lemongrass leaves (Cymbopogon citratus) and stevia leaves (Stevia rebaudiana) which have been explained above, making moringa leaves (Moringa oleifera) and lemongrass leaves (Cymbopogon citratus) and stevia (Stevia rebaudiana) the right combination in herbal tea as a natural treatment for type 2 DM sufferers. Based on the background, the problem in this study can be formulated as: what is the effect of giving a combination of boiled herbal tea with a combination of moringa leaves (Moringa oleifera), lemongrass leaves (Cymbopogon Citratus) and stevia leaves (Stevia rebaudiana) on mice (Mus musculus) induced by alloxan?

RESEARCH MATERIALS AND METHODS

This is a laboratory experimental study with a posttest-only controlled group design in hyperglycemic mice (Mus musculus).

This study used 30 mice as samples, which underwent acclimatization for 2 weeks. After acclimatization, the test animals were randomly divided into 6 groups. Blood glucose levels were then checked using a glucometer (FamilyDr) through the tail as the initial data (before alloxan induction) to exclude mice with abnormal baseline levels.

Data analysis was performed using SPSS software. Results were considered significant if p-value <0.05, followed by post hoc testing.

RESEARCH RESULT

KGD

Table 1. Initial KGD

Kelompok	$\bar{x} \pm SD$ (mg/dL)	p
K1	108,0 ± 12,92	
K2	109,0 ± 12,08	
K3	114,0 ± 15,67	<0,632
K4	110,2 ± 14,72	
K5	121,4 ± 19,13	

The results of the study in Table 4.1 show that after acclimatization, the lowest mouse blood glucose level was in group K1 where the group was only given food and drink normally with an average of 108.0 mg/dL and a standard deviation of 12.92. The highest mouse blood glucose level was in group K5 where the group was also only given food and drink normally with an average of 121.4 mg/dL and a standard deviation of 19.13. The p-value for the initial blood glucose level was <0.633, which means there was no significance so there was no significant difference between the groups.

Table 2. KGD Week 1

Kelompok	$\bar{x} \pm SD$ (mg/dL)	p
K1	110,4 ± 7,13	
K2	119,6 ± 6,19	
K3	122,4 ± 7,92	<0,252
K4	111,6 ± 11,06	
K5	115,2 ±13,24	

After 1 week of HFD administration, the lowest mouse blood glucose was found in group K1 where the group only ate and drank normally with an average of 110.4 mg/dL and a standard deviation of 7.13. The highest mouse blood glucose was found in group K3 where the group was given HFD and ate and drank normally with an average

of 122.4 mg/dL and a standard deviation of 7.92. The p-value for the blood glucose in the first week of HFD administration was <0.252, which means there was no significance so there was no significant difference between the groups.

Table 3. KGD HFD Week 2

Kelompok	$\bar{x} \pm SD$ (mg/dL)	Nilai p
K1	**117,0 ± 8,49**	
K2	128,6 ± 8,40	
K3	**131,6 ± 2,51**	<0,101
K4	118,0 ± 16,00	
K5	117,4 ± 11,01	

After 2 weeks of HFD administration, the lowest mouse blood glucose was found in group K1 where the group only ate and drank normally with an average of 117.0 mg/dL and a standard deviation of 8.49. The highest mouse blood glucose was found in group K3 where the group was given HFD and ate and drank normally with an average of 131.6 mg/dL and a standard deviation of 2.51. The p-value for the blood glucose in the second week of HFD administration was <0.101, which means there was no significance so there was no significant difference between the groups.

Table 4. KGD HFD Week 3

Kelompok	$\bar{x} \pm SD$ (mg/dL)	p
K1	**113,4 ± 8,20**	
K2	121,4 ± 6,73	
K3	**127,2 ± 7,43**	<0,172
K4	118,0 ± 4,95	
K5	121,4 ± 12,93	

After 3 weeks of HFD administration, the lowest blood glucose level in mice was found in group K1 where the group only ate and drank normally with an average of 113.4 mg/dL and a standard deviation of 8.20. The

highest blood glucose level in mice was found in group K3 where the group was given HFD and ate and drank normally with an average of 127.2 mg/dL and a standard deviation of 7.43. The p-value for blood glucose in the third week of HFD administration was <0.172, which means there was no significance so there was no significant difference between the groups.

Table 5. KGD HFD Week 4

Kelompok	$\bar{x} \pm SD$ (mg/dL)	p
K1	**111,6 ± 12,45**	
K2	158,4 ± 18,15	
K3	**172,2 ± 9,71**	<0,001
K4	157,6 ± 9,66	
K5	161,4 ± 12,80	

After 4 weeks of HFD administration, the lowest mouse blood glucose was found in group K1 where the group only ate and drank normally with an average of 111.6 mg/dL and a standard deviation of 12.45. The highest mouse blood glucose was found in group K3 where the group was given HFD and ate and drank normally with an average of 172.2 mg/dL and a standard deviation of 9.71. The p-value for the blood glucose in the third week of HFD administration was <0.101, which means there is significance, indicating that there is a significant difference between each group.

Kelompok (i)	Kelompok (ii)	p
K1	K2	**< 0,001**
	K3	**<0,001**
	K4	**< 0,001**
	K5	**< 0,001**
K2	K3	<0,112
	K4	<0,925
	K5	<0,723
K3	K4	<0,095
	K5	<0,209
K4	K5	<0,653

From the results of the LSD post hoc test, significant differences between groups were

found in group K1, namely the normal group compared to groups K2 (negative control), K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.001.

Table 7. KGD Day 1

Kelompok	x̄ ± SD (mg/dL)	p
K1	107,8 ± 12,56	
K2	193,0 ± 5,00	
K3	193,8 ± 7,73	<0,001
K4	193,4 ± 9,13	
K5	188,8 ± 3,70	

On the 1st day of extract administration after mice were induced with alloxan, the lowest mouse KGD was in group K1 where the group was only given food and drink normally with an average of 107.8 mg/dL and a standard deviation of 12.56. The highest mouse KGD was in group K3 where the group was given a combination of tea with a concentration of 1.8 mg/mL with an average of 193.8 mg/dL and a standard deviation of 7.73. The lowest mouse KGD in the treatment group was in group K5 which was given a combination of tea with a concentration of 7.2 mg/mL with an average of 188.8 and a standard deviation of 3.70. The p-value for KGD after the first day of extract administration was <0.001 which means there is significance so that there is a significant difference between each other between groups.

Table 8. Post Hoc KGD Day 1

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,001
	K4	< 0,001
	K5	< 0,001
K2	K3	<0,881
	K4	<0,941
	K5	<0,431
K3	K4	<0,941
	K5	<0,35
K4	K5	<0,389

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to groups K2 (negative control), K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.001.

Table 9. KGD Day 5

Kelompok	x̄ ± SD (mg/dL)	p
K1	109,0 ± 13,06	
K2	192,2 ± 8,64	
K3	172,2 ± 9,71	<0,001
K4	150,4 ± 16,16	
K5	158,2 ± 14,29	

On the 5th day of extract administration after the mice were induced with alloxan, the lowest mouse blood glucose was found in group K1 where the group was only given food and drink normally with an average of 109.0 mg/dL and a standard deviation of 13.06. The highest mouse blood glucose was found in group K2 where the group was a negative control with an average of 192.2 mg/dL and a standard deviation of 8.64. The lowest mouse blood glucose in the treatment group was found in group K4 which was given a combination of tea with a concentration of 3.6 mg/mL with an average of 150.4 and a standard deviation of 16.16. The p-value for blood glucose after the 5th day of extract administration was <0.001

which means there is significance so that there is a significant difference between each other between groups.

Table 10. Post Hoc KGD Day 5

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,001
	K4	< 0,001
	K5	< 0,001
K2	K3	<0,023
	K4	<0,001
	K5	<0,001
K3	K4	<0,014
	K5	<0,0,97
K4	K5	<0,344

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to groups K2 (negative control), K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value of <0.001. Group K2 had a significant difference when compared to group K3 with a p value of <0.023 and K4 and K5 with a p value of <0.001. Group K3 had a significant difference when compared to group K4 with a p value of <0.014.

Table 11. KGD Day 10

Kelompok	$\bar{x} \pm SD$ (mg/dL)	Nilai p
K1	103,2 ± 14,67	
K2	196,8 ± 10,87	
K3	157,4 ± 22,81	<0,001
K4	138,0 ± 31,42	
K5	138,2 ± 25,15	

On the 10th day of extract administration after mice were induced with alloxan, the lowest mouse blood glucose was found in group K1 where the group was only given food and drink normally with an average of 103.2 mg/dL and a standard deviation of 14.67. The highest mouse blood glucose was found in group K2 where the group was a negative control with an average of 196.8 mg/dL and a standard deviation of 10.87. The lowest mouse blood glucose in the treatment group was found in group K4 which was given a combination of tea with a concentration of 3.6 mg/mL with an average of 138.0 and a standard deviation of 31.42. The p-value for blood glucose after the 10th day of extract administration was <0.001, which means there is significance so that there is a significant difference between each other between groups.

Table 12. Post Hoc KGD Day 10

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,002
	K4	<0,023
	K5	<0,023
K2	K3	<0,012
	K4	<0,001
	K5	<0,001
K3	K4	<0,184
	K5	<0,188
K4	K5	<0,99

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.001, K3 (combination tea with a concentration of 1.8 mg/mL) with a p value <0.002, K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.023. Group K2 had a significant difference when compared to group K3 with a p value <0.012 and K4 and K5 with a p value <0.001.

Table 13. Day 15

Kelompok	x̄ ± SD (mg/dL)	p
K1	**111,2 ± 11,21**	
K2	**196,0 ± 10,22**	
K3	114,0 ± 15,67	<0,001
K4	115,2 ± 12,05	
K5	117,8 ± 15,80	

On the 15th day of extract administration after mice were induced with alloxan, the lowest mouse blood glucose was found in group K1 where the group was only given food and drink normally with an average of 111.2 mg/dL and a standard deviation of 11.21. The highest mouse blood glucose was found in group K2 where the group was a negative control with an average of 196.0 mg/dL and a standard deviation of 10.22. The lowest mouse blood glucose in the treatment group was found in group K3 which was given a combination of tea with a concentration of 1.8 mg/mL with an average of 114.0 and a standard deviation of 15.67. The p-value for blood glucose after the 15th day of extract administration was <0.001, which means there is significance so that there is a significant difference between each other between groups.

Table 14. Post Hoc KGD Day 15

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,742
	K4	<0,638
	K5	<0,439
K2	K3	<0,001
	K4	<0,001
	K5	<0,001
K3	K4	<0,888
	K5	<0,655
K4	K5	<0,76

From the results of the LSD post hoc test, a significant difference between groups was found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.001. Group K2 had a significant difference when compared to groups K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.001.

Table 15. Percentage of Blood Glucose Decrease on Day 5

Kelompok	x̄ ± SD (%)	p
K1	**-2,0 ± 16,46**	
K2	**-78,0 ± 20,61**	
K3	-26,9 ± 56,87	<0,019
K4	-37,5 ± 15,55	
K5	-33,4 ± 26,51	

On the 5th day of extract administration after mice were induced with alloxan, the lowest decrease in the percentage of mouse KGD was in group K2 where the group was a negative control with an average of -78.0% and a standard deviation of 20.61. The highest percentage of mouse KGD reduction was in group K1 where the group was a normal group that was not given treatment with an average of -2.0% and a standard deviation of 16.46. The highest percentage of mouse KGD reduction in the treatment group was in group K3 which was given a combination of tea with a concentration of 1.8 mg/mL with an average of -26.9% and a standard deviation of 56.87. The p-value on the percentage of KGD reduction after the 5th day of extract administration was <0.019 which means there is significance so that there is a significant difference between each other between groups.

Table 16. Post Hoc Percentage of Blood Glucose Decrease on Day 5

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,002
	K3	<0,223
	K4	< 0,088
	K5	< 0,129
K2	K3	<0,019
	K4	<0,055
	K5	<0,036
K3	K4	<0,597
	K5	<0,746
K4	K5	<0,838

From the results of the LSD post hoc test, a significant difference between groups was found in group K1, namely the normal group compared to group K2 (negative control) with a p value of <0.002. Group K2 had a significant difference when compared to group K3 (combination tea with a concentration of 1.8 mg/mL) with a p value of <0.019 and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value of <0.036.

Kelompok	$\bar{x} \pm SD$ (%)	p
K1	2,67 ± 23,16	
K2	-82,5 ± 23,31	
K3	-41,6 ± 34,27	<0,002
K4	-24,5 ± 17,74	
K5	-17,9 ± 34,69	

On the 10th day of extract administration after mice were induced with alloxan, the lowest percentage decrease in mouse KGD was in group K2 where the group was a negative control with an average of -82.5% and a standard deviation of 23.31. The highest percentage decrease in mouse KGD was in group K1 where the group was normal and was not given treatment with an average of 2.67% and a standard deviation of 23.16. The highest percentage decrease in mouse KGD in the treatment group was in group K5 which was given a combination of tea with a concentration of 7.2 mg/mL with an average of -17.9% and a standard deviation of 34.69. The p-value for the percentage decrease in KGD after the 10th day of extract administration was <0.002, which means there is significance so that there is a significant difference between each other between groups.

Table 18. Post Hoc Percentage of Blood Glucose Decrease on Day 10

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,02
	K4	< 0,135
	K5	< 0,251
K2	K3	<0,03
	K4	<0,004
	K5	<0,002
K3	K4	<0,338
	K5	<0,19
K4	K5	<0,712

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.002 and group K3 (combination tea with a concentration of 1.8 mg/mL). Group K2 had significant differences when compared to group K3 (combination tea with a concentration of 1.8 mg/mL) with a p value <0.03, K4 (combination tea with a concentration of 3.6 mg/mL) with a p value <0.004 and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.002.

Table 19. Percentage of Blood Glucose Decrease on Day 15

Kelompok	$\bar{x} \pm SD$ (%)	p
K1	-3,38 ± 11,64	
K2	-81,4 ± 20,53	
K3	2,4 ± 7,75	<0,001
K4	-2,7 ± 8,84	
K5	1.1 ± 6,34	

On the 15th day of extract administration after mice were induced with alloxan, the lowest decrease in the percentage of mouse

KGD was in group K2 where the group was a negative control with an average of -81.4% and a standard deviation of 20.53. The highest percentage of mouse KGD reduction was in group K3 which was given a combination of tea with a concentration of 1.8 mg/mL with an average of 2.4% and a standard deviation of 7.74. The p-value for the percentage of KGD reduction after the 15th day of extract administration was <0.001 which means there is significance so that there is a significant difference between each other between groups.

Table 20. Post Hoc Percentage of Blood Glucose Decrease on Day 15

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,001
	K3	<0,657
	K4	<0,928
	K5	<0,447
K2	K3	<0,001
	K4	<0,001
	K5	<0,001
K3	K4	<0,724
	K5	<0,75
K4	K5	<0,502

From the results of the LSD post hoc test, a significant difference between groups was found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.001. Group K2 had a significant difference when compared to groups K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.001.

BB
Table 21. Initial BB

Kelompok	x̄ ± SD (gr)	p
K1	27,3 ± 3,19	
K2	26,6 ± 2,59	
K3	25,8 ± 4,43	<0,798
K4	**25,1 ± 3,71**	
K5	25,3 ± 1,85	

After acclimatization, the lowest body weight (BW) of mice was found in group K4, which was only given normal food and water, with an average weight of 25.1 grams and a standard deviation of 3.71. The highest BW of mice was found in group K5, which was also only given normal food and water, with an average weight of 27.3 grams and a standard deviation of 3.19. The p-value for initial BW was <0.798, indicating no significant difference between the groups.

Table 22. BB HFD Week 1

Kelompok	x̄ ± SD (gr)	p
K1	**28,3 ± 2,54**	
K2	27,4 ± 2,99	
K3	26,9 ± 4,71	<0,558
K4	**25,4 ± 2,90**	
K5	25,5 ± 1,97	

After 1 week of HFD administration, the highest mouse weight was in group K1 where the group only ate and drank normally with an average of 28.3 grams and a standard deviation of 2.54. The lowest mouse weight was in group K4 where the group was given HFD and ate and drank normally with an average of 25.4 grams and a standard deviation of 2.90. The highest weight among the groups given HFD was in group K2 with an average of 27.4 grams and a standard deviation of 2.99. The p-value for weight in the first week of HFD administration was <0.558, which means there was no significance so there was no significant difference between the groups.

Table 23. BB HFD Week 2

Kelompok	$\bar{x} \pm SD$ (gr)	p
K1	**28,4 ± 1,55**	
K2	28,2 ± 2,27	
K3	28,1 ± 4,12	<0,306
K4	26,2 ± 2,30	
K5	**25,6 ± 1,52**	

After 2 weeks of HFD feeding, the highest weight gain was found in group K1, where the group only ate and drank normally, with an average of 28.4 grams and a standard deviation of 1.55. The lowest weight gain was found in group K5, where the group was given HFD and ate and drank normally, with an average of 25.6 grams and a standard deviation of 1.52. The highest weight gain among the groups given HFD was found in group K2, with an average of 28.4 grams and a standard deviation of 1.55. The p-value for weight gain in the second week of HFD feeding was <0.306, indicating no significant difference between the groups.

Table 24. BB HFD Week 2

Kelompok	$\bar{x} \pm SD$ (gr)	p
K1	**29,5 ± 2,47**	
K2	27,4 ± 3,32	
K3	28,8 ± 3,35	<0,434
K4	26,9 ± 1,82	
K5	**26,2 ± 0,89**	

After 3 weeks of HFD administration, the highest mouse weight was in group K1 where the group only ate and drank normally with an average of 29.5 grams and a standard deviation of 2.47. The lowest mouse weight was in group K5 where the group was given HFD and ate and drank normally with an average of 26.2 grams and a standard deviation of 0.89. The highest weight among the groups given HFD was in group K3 with an average of 28.8 grams and a standard deviation of 3.35. The p-value for weight in the third week of HFD administration was <0.434, which means there was no significance so there was no significant difference between the groups.

Table 25. HFD BB Week 4

Kelompok	$\bar{x} \pm SD$ (gr)	p
K1	29,4 ± 1,82	
K2	31,1 ± 2,00	
K3	**36,0 ± 3,48**	<0,007
K4	**28,4 ± 3,25**	
K5	30,4 ± 3,49	

After 4 weeks of HFD administration, the highest mouse weight was in group K2 where the group was given HFD and ate and drank normally with an average of 36.0 grams and a standard deviation of 3.48. The lowest mouse weight was in group K4 where the group was given HFD and ate and drank normally with an average of 28.4 grams and a standard deviation of 3.25. The p-value for weight in the fourth week of HFD administration was <0.007, which means there is significance so that there is a meaningful difference between each group.

Table 26. Post Hoc BB HFD Week 4

Kelompok (i)	Kelompok (ii)	p
K1	K2	<0,361
	K3	**<0,003**
	K4	<0,601
	K5	<0,608
K2	K3	**<0,017**
	K4	<0,158
	K5	<0,685
K3	K4	**<0,002**
	K5	**<0,008**
K4	K5	<0,305

From the results of the LSD post hoc test, significant differences between groups were found in group K3, namely the normal group compared to group K1 with a p value <0.003, K2 with a p value <0.017, K3 with a p value <0.002, and K5 with a p value <0.008.

Table 4.27 BB Day 1

Kelompok	x̄ ± SD (gr)	p
K1	30,1 ± 1,56	
K2	38,6 ± 4,98	
K3	39,4 ± 3,01	<0,003
K4	35,5 ± 2,34	
K5	37,2 ± 3,58	

On the 1st day of extract administration after mice were induced with alloxan, the lowest mouse weight was in group K1 where the group was only given food and drink normally with an average of 30.1 grams and a standard deviation of 1.56. The highest mouse weight was in group K3 where the group was given a combination of tea with a concentration of 1.8 mg/mL with an average of 39.4 grams and a standard deviation of 4.01. The lowest mouse weight in the treatment group was in group K4 which was given a combination of tea with a concentration of 3.6 mg/mL with an average of 35.5 grams and a standard deviation of 2.34. The p-value for weight after the first day of extract administration was <0.003 which means there is significance so that there is a significant difference between each other between groups.

Table 28. Post Hoc BB Day 1

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,002
	K3	<0,001
	K4	< 0,018
	K5	< 0,004
K2	K3	<0,707
	K4	<0,152
	K5	<0,488
K3	K4	<0,076
	K5	<0,289
K4	K5	<0,443

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.002, K3 (combination tea with a concentration of 1.8 mg/mL) with a p value <0.001, K4 (combination tea with a concentration of 3.6 mg/mL) with a p value <0.018, and K5 (combination tea with a

concentration of 7.2 mg/mL) with a p value <0.004.

Table 29. BB Day 5

Kelompok	x̄ ± SD (gr)	p
K1	30,8 ± 1,15	
K2	38,8 ± 5,19	
K3	36,9 ± 2,15	<0,008
K4	34,2 ± 2,27	
K5	36,3 ± 3,24	

On the 5th day of extract administration after the mice were induced with alloxan, the lowest mouse weight was in group K1 where the group was only given food and drink normally with an average of 30.8 grams and a standard deviation of 1.15. The highest mouse weight was in group K2 where the group was a negative control with an average of 38.8 grams and a standard deviation of 5.19. The lowest mouse weight in the treatment group was in group K4 which was given a combination of tea with a concentration of 3.6 mg/mL with an average of 34.2 grams and a standard deviation of 2.27. The p-value for weight after the 5th day of extract administration was <0.008 which means there is significance so that there is a significant difference between each other between groups.

Table 30. Post Hoc BB Day 5

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,002
	K3	<0,007
	K4	< 0,103
	K5	< 0,012
K2	K3	<0,342
	K4	<0,03
	K5	<0,224
K3	K4	<0,187
	K5	<0,78
K4	K5	<0,291

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value of <0.002 and K3

(combination tea with a concentration of 1.8 mg/mL) with a p value of <0.004. Group K2 had a significant difference when compared to K4 (combination tea with a concentration of 3.6 mg/mL) with a p value of <0.03.

Table 31. BB Day 10

Kelompok	$\bar{x} \pm SD$ (gr)	p
K1	31,9 ± 1,32	
K2	39,4 ± 5,03	
K3	33,4 ± 2,34	<0,011
K4	32,2 ± 2,06	
K5	32,9 ± 4,16	

On the 10th day of extract administration after mice were induced with alloxan, the lowest mouse weight was in group K1 where the group was only given food and drink normally with an average of 31.9 grams and a standard deviation of 1.32. The highest mouse weight was in group K2 where the group was a negative control with an average of 39.4 grams and a standard deviation of 5.03. The lowest mouse weight in the treatment group was in group K4 which was given a combination of tea with a concentration of 3.6 mg/mL with an average of 32.2 grams and a standard deviation of 2.06. The p-value for weight after the 10th day of extract administration was <0.011 which means there is significance so that there is a significant difference between each other between groups.

Table 32. Post Hoc BB Day 10

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,003
	K3	<0,498
	K4	<0,91
	K5	<0,644
K2	K3	<0,01
	K4	<0,003
	K5	<0,006
K3	K4	<0,572
	K5	<0,828
K4	K5	<0,727

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value of <0.003. Group K2 had significant differences when compared to K3 (combination tea with a concentration of 1.8 mg/mL) with a p value of <0.01, K4 (combination tea with a concentration of 3.6 mg/mL) with a p value of <0.003, and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value of <0.006.

Table 33. BB Day 15

Kelompok	$\bar{x} \pm SD$ (gr)	p
K1	32,3 ± 1,15	
K2	39,5 ± 4,42	
K3	30,4 ± 2,77	<0,001
K4	28,8 ± 2,72	
K5	28,3 ± 3,02	

On the 15th day of extract administration after mice were induced with alloxan, the lowest mouse weight was in group K5 which was given a combination of tea with a concentration of 7.2 mg/mL with an average of 28.3 grams and a standard deviation of 3.02. The highest mouse weight was in group K2 where the group was a negative control with an average of 39.5 grams and a standard deviation of 4.42. The p-value for weight after the 15th day of extract administration was <0.001, which means there is significance so that there is a significant difference between each other between groups.

Table 34. Post Hoc BB Day 15

Kelompok (i)	Kelompok (ii)	p
K1	K2	< 0,022
	K3	<0,396
	K4	<0,733
	K5	<0,608
K2	K3	<0,12
	K4	<0,011
	K5	<0,008
K3	K4	<0,239
	K5	<0,18
K4	K5	<0,863

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value of <0.022. Group K2 had significant differences when compared to K4 (combination tea with a concentration of 3.6 mg/mL) with a p value of <0.011 and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value of <0.008.

Percentage of Weight Loss
Table 35. Percentage of Weight Loss on Day 5

Kelompok	$\bar{x} \pm SD$ (%)	p
K1	–14,1 ± 10,09	
K2	–82,6 ± 67,59	
K3	–47,9 ± 38,02	<0,019
K4	–39,01 ± 25,19	
K5	–43,9 ± 15,32	

On the 5th day of extract administration after the mice were induced with alloxan, the highest percentage of weight loss was in group K1, where the group was only given normal food and water, with an average of -14.1% and a standard deviation of 10.09. The lowest percentage of weight loss was in group K2, which served as a negative control, with an average of -82.6% and a standard deviation of 67.59. The highest percentage of weight loss in the treatment group was in group K4, which was given a combination of tea with a concentration of 3.6 mg/dL, with an average of -39.01% and a standard deviation of 25.19. The p-value for the percentage of weight loss after the 5th day of extract administration was <0.111, indicating no significant difference between the groups.

Table 36. Percentage of Weight Loss on Day 10

Kelompok	$\bar{x} \pm SD$ (%)	p
K1	–17,8 ± 12,67	
K2	–50,2 ± 26,41	
K3	-36,4 ± 36,19	<0,354
K4	-31,19 ± 23,08	
K5	-30,0 ± 15,06	

K1: normal, K2: negative control, K3: combination tea with concentration I (1.8 mg/mL), K4: combination tea with concentration II (3.6 mg/mL), K5: combination tea with concentration III (7.2 mg/mL).

On the 10th day of extract administration after alloxan induction, the highest percentage of weight loss was in group K1, which was fed and watered normally, with an average of -17.8% and a standard deviation of 12.67. The lowest percentage of weight loss was in group K2, which served as the negative control, with an average of -50.2% and a standard deviation of 26.41. The highest percentage of weight loss in the treatment groups was in group K5, which was given combination tea with a concentration of 7.2 mg/dL, with an average of -30.0% and a standard deviation of 15.06. The p-value for the percentage of weight loss after the 10th day of extract administration was <0.354, which means there was no significance, so there was no significant difference between the groups.

Table 37. Percentage of Weight Loss on Day 15

Kelompok	x̄ ± SD (%)	p
K1	-19,3 ± 14,61	
K2	**-54,9 ± 17,82**	
K3	-31,7 ± 37,52	<0,041
K4	-14,4 ± 21,83	
K5	**-11,9 ± 10,74**	

On the 15th day of extract administration after mice were induced with alloxan, the highest percentage of mouse weight loss was in group K5 which was given a combination of tea with a concentration of 7.2 mg/dL with an average of -11.9% and a standard deviation of 10.74. The lowest percentage of mouse weight loss was in group K2 where the group was a negative control with an average of -54.9% and a standard deviation of 17.82. The p-value for the percentage of weight loss after the 15th day of extract administration was <0.041, which means there is significance so that there is a significant difference between each other between groups.

Table 38. Post Hoc Percentage of Weight Loss on Day 15

Kelompok (i)	Kelompok (ii)	p
K1	K2	**< 0,002**
	K3	<0,32
	K4	**<0,08**
	K5	**<0,05**
K2	K3	**<0,001**
	K4	**<0,001**
	K5	**<0,001**
K3	K4	<0,416
	K5	<0,297
K4	K5	<0,812

Dari hasil uji post hoc LSD, perbedaan yang bermakna antarkelompok terdapat pada kelompok K1 yaitu kelompok normal dibandingkan dengan kelompok K2 (kontrol negatif) dengan nilai p <0,002, K4 (teh kombinasi dengan konsentrasi 3,6 mg/mL) dengan nilai p <0,08 dan K5 (teh kombinasi dengan konsentrasi 7,2 mg/mL) dengan nilai p <0,05. Kelompok K2 memiliki perbedaan yang

bermakna saat dibandingkan dengan K3 (teh kombinasi dengan konsentrasi 1,8 mg/mL), K4 (teh kombinasi dengan konsentrasi 3,6 mg/mL), dan K5 (teh kombinasi dengan konsentrasi 7,2 mg/mL) dengan nilai p <0,001.

Indeks Lee
Table 39. Lee Index

Kelompok	Rata-rata Hasil *Index Lee*		Persentase Penurunan *Index Lee* (%)	p
	Awal	Akhir		
K1	269,0	281,2	-4,54	
K2	265,0	**309,7**	**-16,87**	
K3	**263,5**	279,1	-5,92	<0,001
K4	266,6	278,7	-4,54	
K5	**269,9**	**275,6**	-2,11	

After acclimatization, the lowest initial lee index of mice was found in group K3 where the group was only given food and drink with an average of 263.5. The highest initial lee index of mice was found in group K5 where the group was only given food and drink with an average of 269.9. After 15 days of extract administration, the lowest final lee index of mice was found in group K5 K5 which was given a combination of tea with a concentration of 7.2 mg/dL with an average of 275.6. The highest final lee index of mice was found in group K2 where the group was a negative control with an average of 309.7. The p-value for the final lee index was <0.001 which means there was significance so that there was a significant difference between each other between groups.

Table 40. Post Hoc Lee Index

Kelompok (i)	Kelompok (ii)	p
K1	K2	**< 0,001**
	K3	<0,716
	K4	<0,671
	K5	<0,338
K2	K3	**<0,001**
	K4	**<0,001**
	K5	**<0,001**
K3	K4	<0,952
	K5	<0,547
K4	K5	<0,588

From the results of the LSD post hoc test, a significant difference between groups was found in group K1, namely the normal group compared to group K2 (negative control) with a p value <0.001. Group K2 had a significant difference when compared to K3 (combination tea with a concentration of 1.8 mg/mL), K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value <0.001.

Liver Organ Index
Table 41. Liver Organ Index

Kelompok	x̄ (%)	p
K1	5,08	
K2	6,53	
K3	5,93	<0,025
K4	6,21	
K5	5,85	

After 15 days of extract administration, the lowest liver organ index of mice was found in group K1, which was the normal group with an average of 5.08%. The highest liver organ index of mice was found in group K2, which was the negative control group that was only given HFD with an average of 6.29%. The lowest liver organ index of mice among the treatment groups was found in group K6, which was given 50 mg/kgBW of moringa leaf ethanol extract and 100 mg/kgBW of chayote ethanol extract with an average of 4.83%. The p-value for the liver organ index was <0.001, which means there was significance so that there was a significant difference between each other between groups.

Table 42. Post Hoc Liver Organ Index

Kelompok (i)	Kelompok (ii)	p
K1	K2	<0,002
	K3	<0,047
	K4	<0,012
	K5	<0,071
K2	K3	<0,16
	K4	<0,444
	K5	<0,112
K3	K4	<0,506
	K5	<0,839
K4	K5	<0,387

From the results of the LSD post hoc test, significant differences between groups were found in group K1, namely the normal group compared to group K2 (negative control) with a p value of <0.002, K3 (combination tea with a concentration of 1.8 mg/mL) with a p value of <0.047, and K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) with a p value of <0.012.

DISCUSSION

KGD
After 4 weeks of HFD administration, there was an increase in blood glucose levels in the negative control (K2) and treatment groups (K3, K4, and K5). In the 4th week of HFD administration, there was a significant difference between groups, namely K1 (normal) and the group given HFD, indicating that HFD can increase blood glucose levels in mice in 4 weeks. According to research from Indriputri, et al., 2022, where Wistar rats were given HFD for 50 days, there was an increase in fasting blood glucose levels in mice after 2 weeks of HFD administration. HFD administration can trigger various disorders such as obesity, dyslipidemia, hypertension, and impaired glucose tolerance. During 15 days of administration of the tea combination, there was a decrease in blood glucose levels. On the 5th day of administration of the tea

combination, there was a significant difference between the K2 group and the treatment groups, namely the K3 group (combined tea with a concentration of 1.8 mg/mL), and K4 (combined tea with a concentration of 3.6 mg/mL), and K5 (combined tea with a concentration of 7.2 mg/mL). Blood glucose reduction was better in group K3 (combination tea with a concentration of 1.8 mg/mL) on day 15. Group K4 (combination tea with a concentration of 3.6 mg/mL) had better blood glucose reduction on days 5 and 10 of combined tea administration. Post hoc test results on day 15 showed a difference between group K2 and the treatment group. The treatment group showed no significant difference compared to group K1 (normal), indicating that the tea combination was effective in reducing blood glucose. The percentage of blood glucose reduction was also better in group K4 (combination tea with a concentration of 3.6 mg/mL) on day 15 compared to the other treatment groups. Post hoc test results on day 15 showed a difference between group K2 and the treatment group. According to research conducted by Owens et al. (2020), administering both ethanol and aqueous extracts of Moringa leaves to experimental animals can reduce blood glucose. According to another study conducted by Vargas-Sanchez et al. In 2019, there was a 34.23% decrease in blood glucose on day 2 and 58.69% on day 3, with $p < 0.01$, in mice after administration of Moringa leaf extract. (61–63)

According to research conducted by Christy et al. (2022), lemongrass leaves, a herb commonly used as a flavoring in food and beverages, were found to have good potential in controlling blood glucose. According to research conducted by Chowdhury et al. (2022), blood glucose levels in test animals were measured on days 1 (baseline), 5 (induction), and 12 (treatment) to determine initial blood glucose levels, after alloxan induction, and after administration of test compounds, including 0.5% CMC Na, glibenclamide, and microencapsulated stevia leaf extract at doses of 100, 300, and 700 mg/kgBW. All three doses of stevia leaf extract were able to reduce blood glucose levels. This was evident from statistical tests showing a significant difference ($p<0.05$) between the CMC group and the Glibenclamide and Stevia leaf extract groups. Stevia leaf extract was able to reduce blood glucose levels at an effective dose of 100 mg/kgBW. (64,65)

The flavonoids contained in these three leaves can lower blood glucose levels by protecting pancreatic β-cells, activating insulin signaling, stimulating the pancreas to secrete insulin, inhibiting glucogenolysis, inhibiting gluconeogenesis, inhibiting digestive enzymes, and inhibiting carbohydrate metabolism enzymes. Flavonoids can reduce insulin resistance in T2DM by regulating the β-AMPK/ACC signaling pathway. Flavonoids can also prevent insulin resistance and metabolic dysfunction, primarily through stimulation of the GALR2-GLUT4 signaling pathway. (66,67)

BW

After a 4-week HFD, there was an increase in body weight, but it was not significant in the negative control (K2) and treatment groups (K3, K4, and K5). In the 4th week of HFD, there was a significant difference with a p-value of <0.007. From the results of the post hoc test, there was only a difference between the K3 group and the K1, K4, and K5 groups. This

indicates that the provision of HFD for 4 weeks has not been able to increase body weight effectively. According to research conducted by Dwi Enggarwati et al. 2023, mice experienced an increase in body weight after being induced by HFD for 8 weeks. During 15 days of administration of the tea combination, there was a decrease in body weight. From the results of the post hoc test, on the 5th day there was a significant difference between the K2 group and the K4 group (combination tea with a concentration of 3.6 mg/mL). On the 10th day there was a difference between the K2 group and the treatment groups, namely the K3 group (combination tea with a concentration of 1.8 mg/mL), and K4 (combination tea with a concentration of 3.6 mg/mL), and K5 (combination tea with a concentration of 7.2 mg/mL) thus indicating that the combination tea was able to reduce body weight effectively. The K5 group (combination tea with a concentration of 7.2 mg/mL) was better at reducing body weight on the 15th day compared to the other treatment groups. Group K5 also had a better percentage of weight loss.

CONCLUSIONS AND SUGGESTIONS

The results of the test on the effects of a combination of boiled herbal tea containing Moringa oleifera leaves, lemongrass leaves (Cymbopogon citratus), and stevia leaves (Stevia rebaudiana) on alloxan-induced mice (Mus musculus) showed the following:

1. The combination tea with a concentration of 3.6 mg/mL significantly reduced blood glucose (BGD) in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.
2. The combination tea with a concentration of 3.6 mg/mL significantly reduced blood glucose in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.
3. The combination tea with a concentration of 7.2 mg/mL significantly reduced body weight in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.
4. The combination tea with a concentration of 7.2 mg/mL significantly reduced body weight in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.
5. A combination tea with a concentration of 7.2 mg/mL significantly reduced the lee index in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.
6. A combination tea with a concentration of 7.2 mg/mL significantly improved the liver index in diabetic mice induced by a HFD and alloxan compared to the other treatment groups.

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