



## Effectiveness of Fig Leaf Extract (*Ficus Carica L.*) in Lowering Blood Glucose in Mice (*Mus Musculus*)

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Received: 24-02-2023

Accepted: 03-03-2023

Published: 27-03-2023

### ABSTRACT

Fig leaves (*Ficus carica L.*) is a plant that has antidiabetic properties, because fig leaves contain alkaloid compounds, flavonoids, tannins, polyphenols, saponins, terpenoids, and steroids. This study aims to determine the extract of fig leaves (*Ficus carica L.*) in lowering blood glucose in mice (*Mus musculus*). Extraction is carried out by maceration with 96% ethanol solvent, then evaporated using Rotavapor. This study used alloxane as a diabetes inducer, the dose of fig leaf extract tested was 5%, 10% and 15% given orally. Observations were made on day 3 and day 7. As a positive control used Glibenclamide and Na. CMC 1% w/v as a negative control. The results showed an average percent reduction in blood glucose levels for negative controls by 18.6%, for 5% extracts by 29.1%, for 10% extracts by 46.6%, for 15% extracts by 83.9% and for positive controls by 45.8%. The results of research have been obtained that the administration of Fig Leaf extract (*Ficus carica L.*) is proven to reduce blood glucose levels in mice (*Mus musculus*) induced by alloxane at concentrations of 5%, 10%, 15%. In the One-way ANOVA test, it shows a significant value ( $p < 0.05$ ) showing a significant difference in each contract. It can be concluded that fig leaves can be a potential alternative treatment for diabetes mellitus with the right concentration can be an effective and natural treatment option.

**Keywords:** alloxan, diabetes, ficus carica l.

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### INTRODUCTION

Diabetes mellitus is the most deadly disease globally (Lampe et al., 2020). This disease causes complications that lead to death. Diabetes mellitus is a disease that cannot be infected. Diabetes is divided into several types: Type I and Type II. Every year, there is always a significant increase (Kurniawaty & Lestari, 2016).

Quoted from the Data and Information Center of the Indonesian Ministry of Health (InfoDATIN) states that Diabetes does not only cause premature death worldwide. This disease is also a significant cause of blindness. Heart disease and kidney failure. The International Diabetes Federation (IDF) estimates that at least 463 million people aged 20-79 years in the world have Diabetes in 2019 or the equivalent of a prevalence rate of 9.3% of the total population at the same age. Based on gender, IDF estimates that the prevalence of Diabetes in 2019 is 9% for women and 9.65% for men. The prevalence of Diabetes is estimated to increase with the increasing age of the population to 19.9% or 111.2 million people aged 65-79 years. The number is predicted to continue to increase until it reaches 578 million in 2030 and 700 million in 2045.

The 2018 Riskeddas results show that the prevalence of Diabetes mellitus in Indonesia based on a doctor's diagnosis at the age of  $\geq 15$  years on the 2013 Riskeddas results is 1.5% (Karyadi, 2022). However, the prevalence of Diabetes mellitus, according to blood sugar examination results, increased from 6.9% in 2013 to 8.5 in 2018. This figure indicates that only around 25% of diabetics know that they have Diabetes (Nova et al., 2020).

The World Health Organization (2018) estimates that around 422 million adults aged over 18 years have been living with Diabetes since 2014. The most significant number are estimated to come from Southeast Asia and the West Pacific, 96 million and 131 million, respectively.

In the world of medicine, this disease can be treated with various kinds of drugs, such as taking medicines made from herbal ingredients or chemical drugs. Treatment efforts to control blood sugar levels and prevent complications in people with diabetes mellitus include using hypoglycemic drugs derived from plants. Ara leaves are plants used in traditional medicine, and fig leaves have many benefits (Adawiyah, 2018).

One of the plants that have antidiabetic activity is the fig or fig fruit, but what is often used from this plant is the leaves to lower blood glucose in the body (WU et al., 2022). Fig leaves are a good source of vitamins A, B1 and B2. Ara leaves also contain calcium, phosphorus, manganese, iron, potassium and sodium. Fig leaves have many health benefits (Maximum, 2020).

Based on research conducted by (Nafiandary, 2019), Fig leaves (*Ficus carica L.*) contain phytochemical compounds belonging to the alkaloid, phenolic, flavonoid and triterpenoid groups, which can treat various health problems such as cancer, diabetes mellitus, vascular and nerve diseases.

Plants are often used directly by the people of Bone, especially in the Lapri area, because they are alternative medicines for the treatment of Diabetes, which have fewer side effects than chemical drugs (Adhikari et al., 2023). Even though fig leaves have been used empirically, if they have not been accepted in the medical world, then fig leaves will still be familiar with people's herbal medicines. Fig leaves without proof will not develop into herbal products that people trust. Researchers are interested in researching fig leaves (*Ficus carica L.*) for their effectiveness. However, further research is needed because many plants have unknown toxicity levels. In addition to Diabetes medication, fig leaves also have properties such as preventing heart disease, anti-cancer, and heart disease (Lestario, 2018).

The purpose of this study was to see the ethanol extract of fig leaves (*Ficus carica L.*) has an effect in lowering blood glucose in mice (*Mus musculus*). The benefit of this study is to provide information to the public about the use of Fig Leaves in lowering blood glucose and as a reference for future research.

## **METHODS**

This research was conducted at the Pharmacology Laboratory and Chemistry Laboratory of the Pharmacy Department of the Health Ministry's Makassar Polytechnic. The time for this research to be carried out is between August 2021- April 2022. This type of research is experimental research conducted to test fig leaf extract (*Ficus carica L.*) obtained from the district. Bone in the Lapri Section to test the effectiveness of reducing blood glucose in mice (*Mus musculus*). The materials used in this study were fig leaves (*Ficus carica L.*) and mice (*Mus musculus*), 96% ethanol, glibenclamide tablets, ammonia, chloroform, H<sub>2</sub>SO<sub>4</sub>, Mayer reagent, Wagner reagent, dragendroff reagent. Concentrated HCl, Mg Powder, FeCl<sub>3</sub>, Acetic Acid, Na-CMC, and alloxan. The tools used in this study were GlucoDr AGM-2100, glucose strips, syringe, analytical balance (*Aicis*), coarse scale (*Ohaus*), stir bar, porcelain cup, measuring cup, maceration vessel, simplicial oven, *rotary evaporator*, tube's reaction, Erlenmeyer 100 ml, mortar, scissors, and alcohol swab. The experimental animals used in this study were mice (*Mus musculus*) healthy males (@ 30 g) totaling 15 heads who were monitored for one week and gave feed and water ad libitum and were divided into 2 groups, namely groups 1 and 5 were control groups (6 mice) which were divided into two groups, namely the positive control group and the negative control group without alloxane inducers. While group 2,3,4 is the treatment group. Furthermore, mice were induced using alloxane at a dose of 3.36 mg / 20 g / 0.5 ml / 20 g administered intraperitoneal and fed and drank for 3 days.

Initial measurement of blood glucose levels was carried out on day 3 and day 7 after administration of the extract. blood collection was carried out through the tail of mice by first satisfying

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mice for 8 hours. Mice are declared diabetic if their fasting blood glucose level is more than 150mg/dL. After the treatment was carried out, the mice were checked again using the GlucoDr AGM-2100 glucometer with previously satisfied for 8 hours. Furthermore, data on glucose levels from male mice (*Muc musculus*) were compiled in tables. The percentage results that have been obtained, then statistical analysis is carried out using the SPSS version 22 test. To see the normality value with the Shapiro-Wilk method, the result shows that the significant value ( $p > 0.05$ ) is a normal distributed value. The test looks at the homogeneity value with the Test of Homoginrtiy of Variences method, the results show Sig values of  $0.56 > 0.05$  which means homogeneous data. The variable inhibitory power test data is homogeny and can be continued for the ANOVA One way test. One way ANOVA test results obtained values of  $0.000 < 0.05$  which means there are significant differences between each treatment group. And then continued with further tests, namely Post Hoc with the Tukey method obtained a significant value ( $p < 0.05$ ) showing a difference between each concentration. Each observation was analyzed using analysis of variant (ANOVA).

## RESULTS AND DISCUSSION

### Results Leaf Extraction Fig (*Ficus carica L.*)

This time, the sample was Ara Leaf (*Ficus carica L.*), taken from the district. Bone, Kususnya in parts area Capri Which picked direct from the tree.

**Table 1. Heavy Extract Leaf Fig (*Ficus carica L.*)**

Sample	Type Solvent	Heavy Sample dry	Heavy Extract	yield	Literature
Leaf Fig ( <i>Ficus carica L.</i> )	Ethanol 96 %	165 grams	91.7 grams	55.57%	< 5.9% (Senduk et al., 2020)

### Results Test Compound Phytochemicals Leaf Extract Fig (*Ficus carica L.*)

**Table 2. Results Observation Screening Phytochemicals Extract Leaf Fig**

Type compound	Change colour	Results	References
Alkaloids	Mayer = precipitate white	(+)	Mayer = precipitate white
	Wagner = precipitate chocolate		Wagner = precipitate chocolate
Flavonoids	precipitate Green	(+)	Green
tannins	Green black	(+)	Green Black
Polyphenols	Black	(+)	Black
Saponins	formed froth	(+)	formed froth
terpenoids	Purplish	(+)	Purple
Steroids	Own black ring	(-)	Blue

### Results of Measuring Blood Glucose Levels in Mice Whichinduced Alloxan

**Table 3. Results of Measuring Blood Glucose Levels in Induced Mice Alloxan**

Group	Replication	Heavy Mice (g)	Sugar Blood	After	Blood Glucose LevelsAfter	
			Beginning (mg/dL)	Induction (mg/dL)	Day The 3rd	7th day
Na.CMC 1% (Control -)	1	29.4 g	75	117	113	110
	2	21.9 g	153	193	189	183
	3	27.2 g	84	112	110	108
	Amount		312	422	412	401
	Average		104	140.6	137,3	133.6
Extract 5%	1	27.2 g	129	152	149	147
	2	26.5 g	134	200	196	172
	3	27.0 g	175	182	179	172
	Amount		438	534	521	491

Group	Replication	Heavy Mice (g)	Sugar Blood	After	Blood Glucose Levels After	
			Beginning (mg/dL)	Induction (mg/dL)	Giving (mg/dL)	Day The 3rd
Extract 10%	Average		146	178	173.6	163.6
	1	30 g	119	247	191	185
	2	26.5 g	130	254	210	198
	3	28.1 g	125	237	220	185
	Amount		374	738	621	568
Extract 15%	Average		124.6	246	207	189.3
	1	31.2 g	125	174	161	133
	2	30.7 g	97	277	259	128
	3	29.8 g	130	189	143	120
	Amount		352	640	563	381
Glibenclamide (Control +)	Average		117,3	213,3	187.6	127
	1	27.6 g	165	200	192	185
	2	19.3 g	125	260	245	195
	3	26.8 g	80	230	200	160
	Amount		370	690	637	364
	Average		123.3	230	212,3	121.3

Average Blood Glucose Levels of Mice at the Beginning, After Induction and Decrease in Blood Glucose

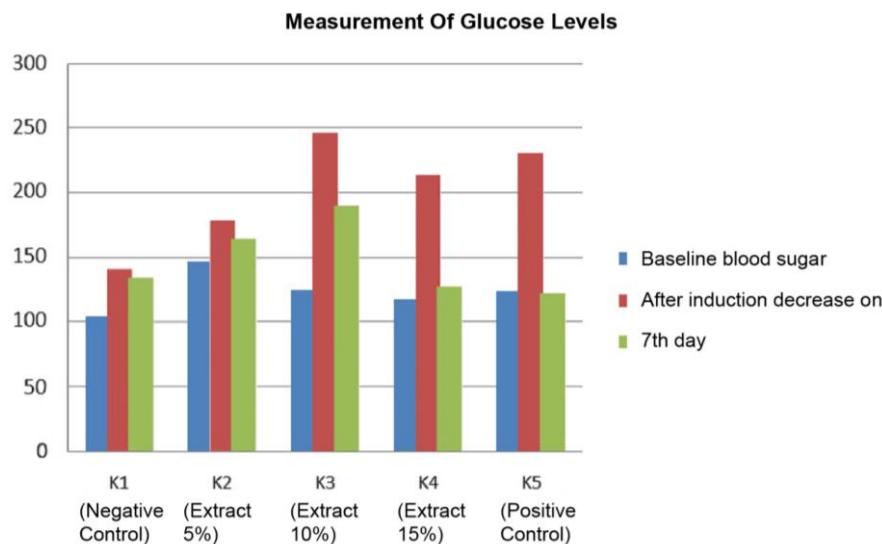
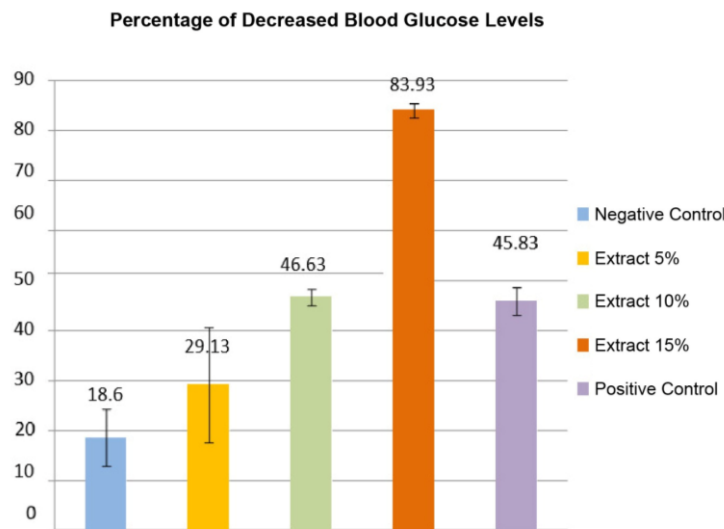


Figure 1. Mean Blood Glucose Levels in Early Mice, After Induction and Decrease in Blood Glucose

Percentage of Decreased Blood Glucose Levels of Mice (*Mus musculus*) as Indicated by Alloxan

Table 4. Percentage of Decreased Blood Glucose Levels in Alloxan-Induced Mice

Replication	Percentage Effect Decline Rate Glucose Blood Mice				
	Control Negative (Na-CMC1%)	Extract Fig leaf( <i>Ficus carica L.</i> )5%	Extract Fig leaf ( <i>Ficus carica L.</i> )10%	Extract Fig leaf ( <i>Ficus carica L.</i> )15%	Positive Control (Glibenkamid)
1	16.6%	21.7%	48.4%	83.6%	42.8%
2	25%	42.4%	45.1%	82.7%	48.1%
3	14.2%	23.3%	46.4%	85.5%	46.6%
<b>Average</b>	<b>18.6%</b>	<b>29.1%</b>	<b>46.6%</b>	<b>83.9</b>	<b>45.8%</b>

**STDEV Results of Blood Glucose Levels in Mice (*Mus Musculus*)**

**Figure 2. The average percentage of blood glucose levels**

Based on the research results, samples of fig leaves (*Ficus carica L.*) are soaked using 96% ethanol. 96% ethanol was chosen as the solvent in this extraction because, according to research conducted by (Nurzahra et al., 2022), the best treatment test results were obtained in the 96% ethanol solvent type treatment. 96% ethanol is a polar compound that quickly evaporates, so it is good to use as an extracting solvent (Kurniawati, 2017). The weight of the dry sample is 165 grams, while the weight of the viscous extract is 91.7 grams, and the yield is 55.57%. Yield is the ratio of dry weight to the number of raw materials. The yield value is related to the amount of bioactive content contained. The higher the yield, the higher the content of substances attracted to raw material. This calculation is carried out to determine the percentage of the amount of material remaining as a result of the extraction process and to determine the effectiveness of the resulting process (Farhan et al., 2022).

Based on the results of the phytochemical screening test of Fig Leaf Extract (*Ficus carica L.*), Alkaloid testing using Mayer's reagent (White precipitate) on Wagner's reagent (brown), it can be concluded that (alkaloid positive) (Meziant et al., 2021). Flavonoid testing showed results (green precipitate) on adding Mg metal and concentrated HCl, concluded (flavonoid positive). The tannin test showed results (blackish Green) after adding FeCl<sub>3</sub> solution and was concluded (tannin positive). Polyphenol testing shows (black colour) concluded (polyphenol positive). The saponin test shows (favourable for the formation of foam) after boiling for 2-3 minutes and cooling, it is concluded (positive for saponins). The terpenoid test showed (purple colour) after adding glacial acetic acid, and it was concluded (terpenoid positive). Steroid testing showed results (formed black rings), and it can be concluded that fig leaves do not contain steroid compounds (Meziant et al., 2021). Therefore, fig leaves contain alkaloids, tannins, flavonoids, polyphenols, saponins and terpenoids. Meanwhile, steroids are not contained in fig leaves (Simaremare, 2014).

In this study, the test animals used were male mice weighing 20-30 g, first adapted to the surrounding environment. Mice were chosen as test animals because they have well-characterized anatomical and physiological characteristics; besides that, they are easy to obtain, easy to handle, inexpensive, and considering that the volume of blood needed to measure blood sugar levels is only tiny, it will be more effective to use mice than other animals. Male mice were chosen because they have a more stable hormone system than female mice. After all, the hormone estrogen in female mice can affect blood glucose levels in the body. Male mice aged 2-3 months are young adult mice with optimal physiological conditions (Khairiyani, 2018). Mice were divided into five groups. Group 1 is negative control (Na-CMC 1%), group 2 is 5% extract, group 3 is 10% extract, group 4 is 15% extract and group

5 namely positive control (glibenclamide), where glibenclamide is an antihyperglycemic drug, sulfonylurea group with a mechanism stimulates insulin secretion.

Table 3 shows the results of observations that have been treated in the five groups of mice. The results of observations of initial blood glucose levels ranged from 75-165 mg/dL before being induced by alloxan. Blood glucose levels after alloxan induction ranged from 117-277 mg/dL. Mice with fasting blood glucose levels  $\geq 150$  mg/dL are declared hyperglycemia and can be used for further studies (Rachmansyah et al., 2020). This shows that alloxan has damaged the pancreatic beta cells of mice. However, when alloxan was given, glucose was not added so that these mice could experience hypoglycemia, so these mice did not experience a significant increase in blood glucose. Based on research conducted by (Kumalasari et al., 2019), giving 5% glucose after alloxan-induced mice aim to prevent the hypoglycemia phase, which can cause seizures and can be fatal.

Table 3 extract ethanol Leaf Fig (*Ficus carica L.*) on concentrations of 5%, 10% and 15% and glibenclamide (positive control). There was a decrease in blood glucose in mice on day three and day seven after the administration of the extract. On Na-CMC1% (negative control), on the day, the 3rd experienced a decrease in blood glucose levels; on the seventh day, it returned decreased because Na-CMC has no effect antihyperglycemic. Increased blood glucose also occurs due to alloxan still working on the last day of measuring mice's blood glucose levels. This is also supported by data on the percentage of reduced blood glucose levels, where the percentage decrease in blood glucose levels of mice for each treatment group, namely the experimental animal group given 1% Na.CMC showed the percentage of glucose levels decreased blood by 16.6%, 25% and 14.2%. In the experimental animal group done extract Leaf Fig 5% experienced a decline rate glucose blood as significant 21.7%, 42.4% And 23.3%. On the group animal tests, those given fig leaf extract 10% decreased by 48.4%, 45.1% and 46.4%. In the test animal group given leaf extract Ara 15% decreased by 83.6%, 82.7% and 85.5%. And rate glucose blood group animal test try Which suspended glibenclamide experience decline as significant 42.8%, 48.1% And 46.6%. Results percentage show that the group mice given extract And glibenclamide (Control positive) were different with a percentage decreased blood glucose only given Na-CMC solution. The pictures show that fig leaf extract with a concentration of 15% decreases blood glucose in mice, which is not much different from glibenclamide (positive control).

The bar chart shows that the blood sugar level before and after induction increased, and after being given treatment, i.e. administration of fig leaf extract, decreased significantly. The inducer used is alloxan because alloxan is fast and can reach the pancreas; its action is preceded by rapid uptake by Langerhans  $\beta$  cells. The formation of reactive oxygen is a primary factor in damage to cells (Surbakti & Khairun, 2015). Giving There was a decrease in the extract. The Ara Leaf extract is suspected of containing. Phytochemicals, namely alkaloids, flavonoids, tannins, polyphenols, saponins, and terpenoids. This is where flavonoid compounds can lower blood glucose levels with the ability as substance antioxidant. Flavonoids are characteristic protective to damage cell  $\beta$  as producer insulin and can increase insulin sensitivity (Liwu et al., 2019). Alkaloids in Leaves Ara (*Ficus carica L.*) have the potential as anticancer and antidiabetic. For Tannins, polyphenols, saponins, terpenoids and steroids contained in Ara Leaf extract can also increase glycolysis which can help lower glucose blood in the body. However, compared to compound flavonoids, it can be concluded that the content of flavonoids is relatively high in the treatment of antidiabetic.

Furthermore, data or results percentage has obtained, then analyzed statistics using test SPSS version 22. For see mark normality with the method *Shapiro-Wilk*, the result indicates that the significant value ( $p > 0.05$ ) is usually distributed. Test mark homogeneity with method *test Of Homoginrtiy of Variances*, the results show a Sig value of  $0.56 > 0.05$ , meaning data homogeneous. Variables data test Power resistor is homogeneous And cannext For test *One way ANOVA*. Results test *One way ANOVA* obtained mark  $0.000 < 0.05$ , which mean exists a difference significant between each treatment group.

And then, proceed with the advanced test, namely *Post Hoc* with the *Tukey method*, obtained a Significant value ( $p < 0.05$ ) showing the difference between each concentration.

Generally, the contraction extract, Which is most effective in lower blood glucose in mice, is a 15% concentration. This matter because fig leaf extract (*Ficus carica L.*) contains compounds active that exist ng content flavonoids Which own antidiabetic ability Which Work in the process of regeneration from the cell beta pancreasAnd increase insulin secretion.

## CONCLUSION

Based on the results of research that has been done, it can be concluded that fig leaves with a concentration of 5%, 10% and 15% have an effectiveness decline in glucose levels blood in mice Which induces alloxan. Ara leaves can be a potential alternative treatment for diabetes mellitus. In treating Diabetes mellitus, especially type 2, lowering blood glucose levels is crucial to avoid more severe complications. Using Ara leaves with the right concentration can be an effective and natural treatment option.

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