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**THE EFFECTIVENESS TEST OF PAPAYA (*Carrica Papaya L*)  
FLOWER EXTRACT ON BLOOD SUGAR LEVEL OF THE  
SUCROSE-INDUCED MALE MICE (*Mus Musculus L.*)**

*Uji Efektivitas Ekstrak Bunga Pepaya (*Carrica Papaya L.*) Terhadap Kadar Gula Darah Mencit (*Mus Musculus L.*) Jantan Yang Diinduksi Sukrosa*

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**Abstract** The papaya (*Carica papaya L*) flower contain flavonoids, tannins, and triterpenoid steroids which function as antidiabetic. This study was conducted to determine the antidiabetic effect of papaya (*Carica papaya L*) flower extract on sucrose-induced male mice. In this study, mice were made diabetic by inducing them with sucrose at a dose of 160 mg/kg BW. A total of 25 mice were grouped homogeneously into 5 groups, consisting of a negative control group (CMC 0.5%), a positive control group (no administration), a group with a dose of 200 mg/kg BW, a group with a dose of 400 mg/Kg. BW, and the group with a dose of 500 mg/Kg BW. Measurement of blood sugar levels of mice was carried out before administration of sucrose, after administration of sucrose and after administration of papaya flower extract. The results showed that the three doses had an antidiabetic effect, and the administration of papaya flower extract at a dose of 200 mg/Kg BW showed a better effect than the negative control.

**Keywords:** *Papaya Flower, Antidiabetic, Flavonoid, Tannin, Triterpenoid*

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**Abstrak** Bunga pepaya (*Carica papaya L.*) mengandung senyawa flavonoid, tanin, triterpenoid steroid yang berfungsi sebagai antidiabetes. Penelitian ini dilakukan untuk mengetahui dari efek antidiabetik pada ekstrak bunga pepaya (*Carica papaya L.*) terhadap mencit jantan yang diinduksi sukrosa. Pada penelitian ini mencit dibuat diabetes dengan diinduksi sukrosa dengan dosis 160 mg/Kg BB. Sebanyak 25 ekor mencit dibagi menjadi 5 kelompok secara homogen, yang terdiri dari kelompok kontrol negatif (CMC 0,5%), kelompok kontrol positif (tidak ada pemberian), kelompok dosis 200 mg/Kg BB, kelompok dosis 400 mg/Kg BB dan kelompok dosis 500 mg/Kg BB. Pengukuran kadar gula darah mencit dilakukan sebelum pemberian sukrosa, setelah pemberian sukrosa dan setelah pemberian ekstrak bunga pepaya. Pada hasil penelitian pada ketiga dosis tersebut memiliki efek antidiabetik, serta pada pemberian ekstrak bunga pepaya dengan dosis 200 mg/Kg BB menunjukkan efek yang lebih baik dibandingkan dengan kontrol negatif..

**Kata Kunci:** *bunga pepaya, antidiabetik, flavonoid, tanin triterpenoid*

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## INTRODUCTION

Diabetes mellitus (DM) can cause hyperglycemia in DM patients. Hyperglycemia in patients with diabetes mellitus that is not well controlled can cause serious disorders of the body system, blood vessels, and especially the nerves (World Health Organization, 2018). Prevention that can be done is to change the patient's lifestyle, such as physical exercise and improving diet (International Diabetes Federation, 2017). Diabetes mellitus can be controlled using four pillars of management. Diet is one of the important things in the four pillars of DM management because patients do not pay attention to balanced food intake. This is what causes an increase in blood sugar in DM patients. Therefore diet can prevent an increase in blood sugar, and a proper diet can help control blood sugar levels (Soegondo, 2015).

The classification of DM based on etiology according to Perkeni (2015) is as follows: (1) Diabetes mellitus type 1: Diabetes mellitus that occurs due to damage or destruction of beta cells in the pancreas. This situation results in absolute insulin deficiency. There are two types of beta cell damage, autoimmune and idiopathic. (2) Diabetes mellitus type 2: Diabetes mellitus type 2 occurs due to insulin resistance. Insulin is present in sufficient amounts but cannot work optimally resulting in high blood sugar levels in the body. (3) Diabetes mellitus of other types: This DM can occur due to genetic effects of beta cell function, exocrine disease of the pancreas, genetic defects in insulin work, drugs, infections, chemicals, immunological disorders, and other genetic syndromes related to DM. (4) Gestational diabetes mellitus (Perkeni, 2015).

Diabetes mellitus is one type of non-communicable disease that is a serious public health problem in Indonesia and the world. This non-communicable disease diabetes is one of the main causes of blindness, heart attack, kidney failure, leg amputation, and stroke. Based on data from the International Diabetes Federation (IDF) in 2017, adult patients with DM in the world in 2017 reached 425 million of ages between 20-79 years. Data in the Regional Health Research (Risksedas) shows that the prevalence of patients with diabetes in East Java is in the top 10 in Indonesia with a

prevalence of 6.8% (Kominfo Jatim, 2015).

The prevalence of type II diabetes mellitus is increasing rapidly in Asian populations, especially in countries with very fast economic growth. China and India are in the top ranking of the 10 countries with diabetes epidemics, including the Philippines, Bangladesh, Indonesia and Pakistan. An increasing prevalence of type II diabetes can occur in young adults in the 20 to 30 year age group. This high increase is in line with an increase in obesity, which is a major risk factor for type II diabetes (Lim, 2016).

The prevalence of diabetes in Southeast Asia in 2015 as a percentage of adults with diabetes was 8.5%. Indonesia is ranked seventh in the world for the highest prevalence of diabetes in the world along with India, China, America, Brazil, Russia and Mexico with 10 million people suffering from diabetes. Diabetes accompanied by complications is the third leading cause of death in Indonesia. In 2014, there were 96 million adults with diabetes in 11 member countries of the Southeast Asia region with a prevalence of 8.6%. In 2013, diabetes was one of the diseases that caused the largest health expenditure in the world, namely around 612 billion dollars. The prevalence of diabetes tends to increase, namely 5.7% (2007) to 6.9% (2013). The prevalence of overweight is 13.5% (Risksedas, 2013) and obesity is 15.4% (Risksedas 2013) which is one of the main factors causing the increase in diabetes compared to Risikesdas 2007 and 2010 (WHO, 2015).

The most important management of diabetes mellitus is lifestyle changes such as adjusting a healthy and balanced diet (Chatterje, et al, 2018). Diet is one of the main components of success in diabetes management, but there are often obstacles in diabetes services because compliance and motivation from the patients themselves are needed (Setyorini, 2017). Knowledge is needed to reduce the impact caused by diabetes mellitus (Chen, et al., 2015). Self-management is very useful in efforts to develop patient skills to increase self-efficacy (Zainudin, Abu Bakar, Abdullah, & Hussain, 2018). This is expected to minimize the occurrence of acute or chronic complications (Setyorini, 2017).

One of the medicinal plants is papaya

(*Carica papaya*). Papaya is a plant that as a whole has many benefits, be it roots, leaves, flowers, fruit or seeds. Apart from being a plant that can be consumed by humans and animals, papaya plants also have various properties, including extracts of papaya root water for wound healing, and papaya seeds for reducing cholesterol and blood sugar levels. Papaya flowers are usually boiled and then used to treat diabetes mellitus, improve appetite, and cure jaundice. Papaya flowers contain flavonoids, triterpenoid steroids, tannins, and carbohydrates (Ginting, 2017).

## RESEARCH METHOD

### *Population and Setting*

This research is a laboratory experimental study in vivo. The research design chosen was in the form of the True Experimental- Post Test Only Control Group Design which used male mice (*M. musculus* L.) as the research object.

The research was conducted in August - September 2020 at the Ellio Laboratory, Jl. Ngumban Surbakti No.79, Sempakata, Medan city.

The study population was male mice (*M. musculus* L.). Samples were determined by inclusion and exclusion criteria. The inclusion criteria that must be met are as follows: i) healthy male mice (*M. musculus* L.), ii) 2-3 months old, iii) body weight  $\square$  20-30 grams, and iv) no anatomical abnormalities were found, whereas the exclusion criteria were experimental mice were sick or died before the treatment was carried out.

The sample size refers to the WHO (World Health Organization) guidelines regarding the use of experimental animals for research. The minimum number of mice for each treatment group is 5. The sample used in this study consisted of 25 mice (*M. musculus*) because there were 5 groups.

### *Tools and Materials*

The tools used in this experiment are glassware, oven, incubator, blender, test tube, analytical balance, 5 ml syringe, glucometer, and glucose strips.

The materials used in this experiment were mice, papaya flowers, ethanol, sucrose, carboxy methyl cellulose (CMC), aquadest, and animal feed.

### *Procedure*

The papaya flower extract is made using

the maceration method because the maceration method is easier, simpler, and without using special tools. A total of 200 g of papaya flower powder were separately put into a 1000 mL beaker and extracted with 1 L of 96% ethanol. Ethanol is relatively cheap, easy to obtain, and the extract obtained is not easily grown by fungi and bacteria. Maceration is done for 3 days and stirring must be done every day. Stirring aims to increase the number of yields produced (Depkes RI, 2000).

The maceration results obtained are then evaporated using a vacuum rotary evaporator to produce a liquid extract. Vacuum rotary evaporator is used because it is able to facilitate the evaporation of solvent from the macerate sample. Furthermore, the samples were stored in a porcelain dish and then concentrated using a water bath at a temperature of 600°C. The thick extract obtained is then stored in a desiccator to remove the water content from the extract (MOH, 2014).

A sample of 25 *M. musculus* mice was divided into 5 groups, each of which consisted of 5 mice, grouped randomly. All mice were induced by sucrose at a dose of 160 mg/Kg. The blood glucose level of mice is said to be diabetes, which is  $>$  200 mg/dL. Group 1 was assigned as control.

The five Wistar groups are as follows:

- Group I was a negative control, the test animals were given 0.5% Na CMC suspension
- Group II was a positive control group where there were mice induced by sucrose without extract administration
- Group III is treatment 1 (P1), namely diabetic mice with the administration of papaya flower extract of 200 mg/Kg BW / day p.o.
- Group IV is treatment 2 (P2), namely diabetic mice with the administration of papaya flower extract of 400 mg/Kg BW / day p.o.
- Group V is treatment 3 (P3), namely diabetic mice with administration of papaya flower extract of 500 mg/Kg BW / day p.o. (Wahyuni, 2018).

Glucometry is a technique used to obtain glucose concentration values in peripheral or central blood. The measurement value obtained can be expressed by mg/dl which has a very important clinical value to determine whether

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or not there are metabolic disorders such as diabetes mellitus or several other disorders such as malabsorption syndrome, hyperosmolar coma and hypoglycemia, which is a condition when glucose levels are lower than normal levels.

In the papaya flower (*Carica papaya L*) effectiveness test on reducing blood glucose levels, *M. musculus* mice were first induced with a 10% sucrose solution. Sucrose is given because a high-sucrose diet can lead to obesity and type 2 diabetes mellitus, and can cause insulin work disruption through the effect of sucrose on the liver.

Before the administration of sucrose, it is necessary to measure the blood glucose level first. After sucrose was given, the measurement of blood glucose levels was carried out again on day 10, then the *M. musculus* mice were assessed whether they had diabetes or not. Normal blood glucose levels in male *M. musculus* are 71-124 mg / dl (Soemaedji, 2014)

**Data Analysis**

The data obtained in this study were analyzed statistically using the normality test, homogeneity test, paired T-test, one- way ANOVA test, and simple linear regression test.

The hypotheses proposed and tested in this research data analysis are:

Ho: There is a decrease in blood glucose levels of mice after administration of papaya flower extract.

Ha: There was no decrease in blood glucose levels of mice after administration of papaya flower extract.

**RESULTS AND DISCUSSION**

**Results**

Before the treatment in the form of administration of papaya flower extract was carried out, the mean body weight of mice in all groups was measured and the results of this measurement are shown in Table 1.

**Table 1. Baseline Mean Body Weight of Mice**

No.	Group	Mean Body Weight (gr)
1	Positive Control	30.4 ± 9.3
2	Negative Control	29 ± 5.75
3	Treatment 1	29.2 ± 5.5
4	Treatment 2	27.2 ± 8.7
5	Treatment 3	23.6 ± 13.3

Then the blood glucose levels of mice were measured at baseline, pretest, and posttest and the mean blood glucose levels obtained were as shown in Table 2.

**Table 2. Mean Blood Glucose Levels of Mice at Baseline, Pretest, and Posttest**

Group	Number	Mean Glucose Level at <i>Baseline</i>	Mean Glucose Level at <i>Pretest</i>	Mean Glucose Level at <i>Posttest</i>
Control (+)	5	107 ± 36.5	202.6 ± 52.3	172.4 ± 14.8
Control (-)	5	114.6 ± 137.8	203 ± 65.75	196.2 ± 25.63
Treatment 1	5	119.8 ± 13.7	224.6 ± 21.3	149.4 ± 22.3
Treatment 2	5	128 ± 6.5	199.2 ± 20.2	146.4 ± 14.8
Treatment 3	5	108 ± 111.5	200.2 ± 12.7	158.4 ± 2.3
Total	25			

**Table 3. The percentage increase in blood glucose levels of mice after being induced by sucrose**

Group	Mean Glucose Level at <i>Baseline</i>	Mean Glucose Level at <i>Pretest</i>	Average Increase (%)
Control (+)	107 ± 36.5	202.6 ± 52.3	95.6 ± 9.9
Control (-)	114.6 ± 137.8	203 ± 65.75	88.6 ± 17.17
Treatment 1	119.8 ± 13.7	224.6 ± 21.3	98.8 ± 11.88
Treatment 2	128 ± 6.5	199.2 ± 20.2	71.2 ± 5.93
Treatment 3	108 ± 111.5	200.2 ± 12.7	92.2 ± 9.23

The increase in blood glucose levels of mice after being induced by sucrose can be calculated

by the following formula:

$$\%increase = \frac{Pretest\ Glucose - baseline\ glucose}{baseline\ glucoe} \times 100\%$$

The results of the complete calculation of the increase in blood glucose levels in mice are shown in Table 3 above.

It was found that the increase in blood glucose levels in the positive control group was 95.6%, in the negative control group it was 88.6%, in the treatment group at the extract dose of 200 mg/Kg BW was 98.80%, in the treatment

group at the extract dose of 400 mg/Kg BW was 71.2%, and in the treatment group at the extract dose of 500 mg/Kg BW was 92.2%. So it can be concluded that all groups experienced an increase in blood glucose levels after being induced by sucrose. Furthermore, the decrease in blood glucose levels after treatment can be determined using the following formula:

$$\%decrease = \frac{Pretest\ Pretest - baseline\ posttest}{baseline\ glucoe} \times 100\%$$

The results of the complete calculation of the decrease in blood glucose levels for each group of mice are shown in Table 4.

It can be seen in Table 4 that the decrease in blood glucose levels after treatment in the positive control group was 30.2%, in the negative control group it was 7.00%, in the treatment group at extract dose of 200 mg/Kg BW was 69.2%, in the negative control group treatment at the extract dose of 400 mg/Kg BW was 52.8%, and in the treatment group at the

extract dose of 500 mg/Kg BW was 41.8%.

Furthermore, paired T-tests were used to find out whether there was a significant increase in data from the baseline to pretest groups, and also to determine whether there was a significant decrease in data from the pretest and posttest groups. It should be noted that the paired T-test was carried out after the data passed the normality and homogeneity tests

**Table 4. The Average Decrease in Blood Glucose Levels of Mice after Treatment**

Group	Number	Mean Glucose Level at <i>Pretest</i>	Mean Glucose Level at <i>Posttest</i>	Average Increase (%)
Control (+)	5	202.6 ± 52.3	172.4 ± 14.8	30.2 ± 7.01
Control (-)	5	203 ± 65.75	196.2 ± 25.63	7.00 ± 7.78
Treatment 1	5	224.6 ± 21.3	149.4 ± 22.3	69.2 ± 15.09
Treatment 2	5	199.2 ± 20.2	146.4 ± 14.8	52.8 ± 2.05
Treatment 3	5	200.2 ± 12.7	158.4 ± 2.3	41.8 ± 2.59

In the paired T-test between baseline and pretest data, the value of p = 0.000 (p < 0.05) was obtained, which means that there was a significant increase in blood glucose levels after being induced by sucrose. Meanwhile, in the paired T-test between the pretest and posttest data the value of p = 0.00 (p < 0.05) was obtained, which means that there was a significant decrease after treatment.

Then the one-way Anova test was used to determine the differences between groups which numbered more than two treatment groups. The criterion for this test is if the p value is < 0.05, then at least there are data in the

two groups that have significant differences. One-way Anova test was performed on the data on the percentage of blood sugar levels posttest to pretest and a p-value = 0.00 (p < 0.05) was obtained which can be concluded that in the treatment there were at least data from the two groups that were significantly different.

As an advanced statistical test, a simple linear regression test was used to test the significance of the difference in mean data between treatment groups. Based on the results of statistical analysis using the regression test, the significance value = 0.000 was obtained. In accordance with the provisions, if the

significance value  $< \alpha = 0.05$ , it can be stated that various different concentrations of papaya flower extract have a significant effect on blood sugar. Based on this analysis a t-counted value of 9.657 was obtained. Because the t-counted value  $= 9.657 > 2.060$ , it can be concluded that  $H_0$  is rejected and  $H_a$  is accepted, namely "there is an effect of papaya flower extract on the reduction in blood sugar levels".

To determine the effect of papaya flower extract on blood sugar levels, an analysis of the coefficient of determination or symbolized by  $R^2$  is carried out which is the result of testing a decrease in blood sugar levels. From the simple linear regression analysis carried out, it was found that the R-square value was 0.66 or 66%. This value concluded that the papaya flower extract concentration caused a decrease in blood sugar levels of mice by 66%.

### Discussion

There are chemical components in papaya flowers and leaves that are used for the health of the human body, including papaya acetone extract containing steroid molecules (Latifah and Syahril, 2007) and in the ethanol extract of papaya leaves there are alkaloids, tannins and flavonoids (Mahatrinny et al. 2014). Phytochemical analysis of papaya leaves indicates the presence of flavonoids, alkaloids, tannins, saponins and steroids (Ayoola & Adeyeye, 2010). According to Indrawati et al (2002), in papaya flowers there are classes of flavonoids, steroids / triterpenoids, tannins, and carbohydrates.

Flavonoids are antioxidants that can prevent the formation of AGE chains (advanced glycosylation end products) that cause pathological changes in hyperglycemia (Salem, 2009). Alkaloids and tannins are also able to inhibit glucose absorption in the intestine. Thus, alkaloids, flavonoids, and tannins can provide good and beneficial effects in diabetes mellitus conditions.

This is consistent with previous research conducted by Wahyuni et al. In 2018 that papaya (*Carica papaya L.*) flowers contain secondary metabolites such as flavonoids, tannins, steroids and terpenoids. Papaya (*Carica papaya L.*) flower extract has antidiabetic potential at doses of 400 mg/Kg BW and 500 mg/Kg BW which are effective in reducing blood glucose levels in mice

(Wahyuni et al, 2018).

This is in accordance with previous research conducted by Lili Pupas Dewi in 2019. Based on research conducted by Lili Pupas Dewi, it can be concluded that papaya (*Carica papaya L.*) seed extract at a dose of

75 mg/Kg BW, 150 mg/Kg BW, and 300 mg/Kg BW can reduce blood glucose levels in male white rats (*Rattus novergicus*) of Wistar strain that have been induced by alloxan. The optimal dose of papaya seed extract (*Carica papaya L.*) for reducing blood glucose levels in male white rats (*Rattus novergicus*) of Wistar strain that has been induced by alloxan is a dose of 150 mg/Kg BW (Lili Puspa Dewi, 2019).

### CONCLUSIONS

The conclusions that can be drawn in this study are as follows:

1. The results indicated that the most effective treatment to reduce blood sugar levels was papaya flower extract treatment at a dose of 200 mg/kg BW which reduced blood glucose levels by 69.2%.
2. Paired T-test which was conducted between the pretest and posttest data showed the results that "There was a significant decrease after administration of papaya flower extract to reduce blood sugar levels".
3. Based on the results of the study it can be concluded that "there is an effect of papaya flower extract on reducing blood sugar levels".
4. The results showed that the concentration of papaya flower extract to reduce blood sugar levels of mice was 66% on average.

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