Effect of Brotowali Extract Fortification of Papaya Leaves And Sugar Cane Caries on Diabetes Mellitus Type II

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Abstract. Diabetes Mellitus Type II is a metabolic disorder characterized by an increase in blood sugar due to decreased insulin secretion by pancreatic beta cells or impaired insulin function (insulin resistance). Risk factors for diabetes mellitus are age, sex, obesity, hypertension, genetic, food, smoking, alcohol, and lack of activity. Increasing cases of diabetes in Indonesia is a concern that must be followed up in real terms, especially for educators starting from the stage of detection to treatment to reduce prevalence. Diabetes Mellitus Type II is the focus of attention because it is a non-communicative disease that can be prevented through by changes of healthier lifestyle. In the prevention and treatment of Diabetes Mellitus Type II can utilize several types of local medicinal plants, namely brotowali plants, papaya and sugar cane which have antidiabetic substances. This study aims to determine the effect of brotowali fortification extracts of papaya leaves and sugar cane juice induced in mice (Mus musculus). This type of research is an experimental study that was be held in Laboratory of Department Biology Makassar State of University. Brotowali extract of fortified papaya leaves and sugar cane extract at a dose of 250 mg / kg BW and 500 mg / kg BW orally by mixing in drinking water of mice. Brotowali extract of fortified papaya leaves and sugar cane juice is expected to reduce blood glucose levels in mice. The results of this study will be used as a reference or reference in making Diabetes Mellitus Type II drugs from various types of herbal plants including extracts of fortification brotowali, papaya leaves and sugar cane juice.

Keywords: Diabetes Mellitus Type II, Brotowali, Papaya Leaves, Sugar Cane.

1. Introduction

Diabetes mellitus is a disease characterized by the occurrence of hyperglycemia and impaired metabolism of carbohydrates, fats, and proteins associated with an absolute or relative deficiency of work and / or insulin secretion. The International Diabetes Federation (IDF) states that the prevalence of Diabetes Mellitus in the world is 1.9% and has made Diabetes Mellitus the seventh leading cause of death in the world while in 2012 the number of diabetes mellitus in the world is 371 million people where the proportion of diabetes mellitus type 2 is 95% of the world population suffering from diabetes mellitus. The high prevalence of type 2 diabetes mellitus is caused by unchanging risk factors such as sex, age, and genetic factors, the second is a risk factor that can be changed, for example smoking habits level 1.8 [1].

β cells are cells located on the islets of the pancreas Langerhans, tasked with secreting the hormone insulin. Ss cell damage can reduce the secretion of the hormone insulin, this can interfere with the
utilization of food substances in the form of glucose by cells. Glucose will remain in the blood vessels causing glucose levels in the blood to increase. Lack of the hormone insulin can cause diabetes mellitus. Diabetes Mellitus is referred to as “The Silent Killer” because it attacks the organs in the body secretly without showing scary symptoms [2]. Symptoms of DM such as eating a lot (polyphagia), drinking a lot (polydipsia), and a lot of urine (polyuria). World Health Organization (WHO) states there are 347 million people globally diagnosed with diabetes. WHO estimates that DM will be the number seven cause of death worldwide in 2030. In 2011, Indonesia ranked 10th for the highest diabetes cases in the world with 7.2 million sufferers and in 2013 rose to No. 9 in 2013 with 8.5 million sufferers. Currently, Indonesia is still ranked and it is estimated that the number of diabetics will continue to grow until the coming year [2,3].

Cures for diabetes are still being developed, medicines can come from chemicals or from natural ingredients such as plants that have antidiabetic content. Some types of plants that are known to have antidiabetic substances include brotowali plants, papaya and sugar cane itself. Brotowali plants are wild plants in the forest, fields or planted near fences. In general, the brotowali plant contains a variety of chemical compounds, including alkaloids, soft resin, starch, glycosides, picroteosides, harsa, bitter substances pikroretin, tinokrisposid, berberine, palmitin, kolumbin and kaokulin [4]. While papaya plant extracts have been shown to have the effect of reducing hyperglycemic conditions in mice induced by diabetes [5], although so far the active substance has not been identified in the papaya plant, but it is thought that alkaloids, saponins, and tannins are bioactive substances that play a role in this mechanism [6,7]. Meanwhile sugarcane juice has anti-diabetic effect. Sugarcane juice contains sakar, which is an antidiabetic compound [8]. The aim was to determine the effect of papaya leaf brotowali extract and sugar cane extract on type 2 diabetes mellitus. Therefore, the proposer team was interested in examining how the effect of papaya leaf brotowali extract and cane juice extraction on type 2 diabetes mellitus tested on test animals (mice).

2. Experimental method
This type of research is an experimental study conducted at the Biology Laboratory of Faculty of Mathematics and Natural Sciences Makassar State University. This study used 30 male mice (Mus musculus). There are weighing 25 ± 30 grams, 2 months old ICR strain. Mice (Mus musculus) were grouped into 6 treatment groups and each treatment group consisted of 5 replications. Brotowali extract of fortified papaya leaves and sugar cane extract at a dose of 250 mg / kg body weight and 500 mg / kg body weight orally by mixing in drinking water of Mice (Mus musculus). The brotowali fortified papaya leaves and sugar cane extract is expected to reduce blood glucose levels in alloxan-induced Mice (Mus musculus) to get the hyperglycemia condition. First step we make an extract of Brotowali and Papaya leaves with used ethanol 95% solutions, and than we mixing all the extract with sugarcane juice. After we get an extraction, we applied to the mice after induced the alloxan to get the hyperglycemia condition of Mice (Mus musculus). The results of this research will be obtained products in the form of brotowali extract, papaya leaf extract and sugar cane juice and the analyze data used Complete Random Design (CRD) with 5 replications. The results of this study will be used as a reference in making diabetes mellitus type 2 medicine from various types of herbs including brotowali fortification extracts of papaya leaves and sugar cane juice.

3. Experimental Result
The results of the study in Table 1 showed the first step measurement after alloxan induction, all treatment groups were normal control group, medicine control group, group given brotowali fortification extract of papaya leaves and sugarcane extract at a dose of 250 mg / kg BW, and 500 mg / kg BW male mice with an average the highest total glucose level (mg / dL) was produced by the EBFPT 500 mg / kg BW treatment group, which was 210 mg / dL. As for the average total glucose level (mg / dL) the lowest in the EBFPT group is 250 mg / kg BW, which is 206 mg / dL.
Table 1. Average blood glucose level (mg / dL) of mice

| No | Treatment                  | Average blood glucose levels (mg / dL) of male mice |
|----|----------------------------|---------------------------------------------------|
|    |                            | 1st day   | 3rd day | 5th day |
| 1  | Control                    | 160       | 160     | 161     |
| 2  | Medicine (Analog Insulin)  | 200       | 181     | 168     |
| 3  | EBFPT 250 mg/kg WB         | 206       | 194     | 185     |
| 4  | EBFPT 500 mg/kg WB         | 210       | 187     | 177     |

In the second step of measurement after alloxan induction all treatment groups were normal control groups, medicinal control groups, groups that were given extract of fortified brotowali papaya leaves and sugarcane extract at a dose of 250 mg / kg BW, and 500 mg / kg BW male mice with an average the highest total glucose level (mg / dL) is produced by the treatment group EBFPT 250 mg / kg BW, which is 194 mg / dL. Whereas the average total glucose level (mg / dL) was lowest in the EBFPT 500 mg / kg BW group, which was 187 mg / dL.

In the third step after alloxan induction all treatment groups were normal control groups, medicinal control groups, groups that were given brotowali fortification extracts of papaya leaves and sugarcane extract at a dose of 250 mg / kg BW, and 500 mg / kg BW male mice with an average the highest total glucose level (mg / dL) was produced by the treatment group EBFPT 250 mg / kg BW, which is 185 mg / dL. Whereas the average total glucose level (mg / dL) was lowest in the EBFPT 500 mg / kg BW group, which was 177 mg / dL.

Measurements after alloxan induction resulted in a mean total blood glucose levels that were significantly different between the normal control group and the medicinal control group and the EBFPT 250 mg / kg BW treatment group and also produced an average blood glucose level that was very significantly different between the normal control group with treatment of EBFPT 500 mg / kg body weight. Measurement after fortification of Brotowali papaya leaf extract and sugar cane extract showed significantly different results between the normal control group and the medicinal control group.

![Figure 1](image-url)  
*Figure 1. Average blood glucose levels (mg / dL) of male mice on days 1, 3 and 5 after treatment*

Figure 1 showed that decreased blood sugar levels of mice (Mus musculus) in each treatment after brotowali extract fortification of papaya leaves and sugar cane juice administered orally for 5 days obtained results that showed that in normal control there was no significant change because in this group no treatment was given. The treatment group with the extract of fortified brotowali papaya
leaves and sugarcane extract at a dose of 250 mg / kg BW decreased blood sugar levels by 21 mg / dL and the treatment group who were given the extract fortification brotowali papaya leaves and cane juice extract 500 mg / kg BW decreased sugar levels blood by 33 mg / dL. Decreased blood sugar levels in drug control (insulin analog) that is equal to 32 mg / dL. While the biggest decrease in blood sugar levels between all groups was found in the treatment group who were given brotowali extract fortification of papaya leaves and sugarcane juice with a dose of 500 mg / kg BW decreased blood sugar levels by 33 mg / dL. This indicates that there is an effect of brotowali fortification extract of papaya leaves and sugar cane juice on the glucose level of mice. The brotowali extract of fortification of papaya leaves and sugarcane extract at a dose of 500 mg / kg BW showed significant results.

This is in accordance with an experiment conducted by Jaya 2015 which states that Brotowali is one of the medicinal plants that has the potential to be developed. Brotowali is a kind of traditional medicinal plant that usually grows in the yard or in the forest. These vines are usually used as a basis for making traditional herbal medicine, because the content of chemicals in them is believed to be able to provide good benefits for health. This plant is a functional plant because all parts of the plant can be used both for body care and to treat various diseases, besides brotowali Tinospora crispa (L). MIERS is useful to reduce sugar levels, because brotowali plants have antidiabetic properties [9].

According to Indrawari, papaya leaves are commonly used to relieve menstrual pain in women, treat acne, improve digestion, increase appetite, and treat dengue fever. papaya flowers are usually boiled and used for diabetes mellitus (diabetes) [5,6]. Papaya flowers contain flavonoids, tannins, steroids-triterpenoids, and carbohydrates. In addition, based on research conducted by Sitorus, 2012 [10] papaya flowers can also be as antimutagenic in male mice. Many studies show the benefits of papaya plants as anti-diabetes, including research conducted by Sholhah, 2013 [11] showing that the effect of avocado seeds and papaya seeds in mice showed a decrease in blood glucose levels in mice. Research conducted by Venkateshwarlu, 2013 [8, 7] shows that papaya seed extract shows antidiabetic activity. Papaya leaves also contain chemical compounds consisting of alkaloids and sapoin. In addition, papaya leaves also contain the enzymes papain, alkaloids karpaim, pseudocarpin, glycosides, carposids and saponins. The variety of nutrients on papaya leaves has the ability to cure diseases, one of which is diabetes.

According to Hariana, 2013 [8] states that sugarcane juice or usually often referred to as sugar cane juice is one of the traditional drinks which is now much loved by the community. In this sugar cane juice does not contain harmful saturated cholesterol. The substances contained in sugarcane juice are phosphorus, potassium, iron, calcium and magnesium. Sugarcane juice is the result of the feeling that sugarcane stems actually do no harm to diabetics. Precisely this sugar cane was allegedly able to reduce blood sugar levels in diabetics. Because sugarcane juice has a relatively lower glycemic index. So it's safe consumed and helps control normal blood sugar levels.

4. Conclusion
This indicates that there is an effect of brotowali fortification extract of papaya leaves and sugarcane juice on glucose levels of mice. Brotowali extract of fortified papaya leaves and 500 mg / kg BW sugarcane extract showed significant results than Brotowali extract of fortified papaya leaves and 250 mg / kg BW sugarcane.

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