**The Potential of Chinese Ketepeng (*Cassia alata* L) Cook Water On Streptozotocin Induced Blood Sugar Decrease of Mice (*Mus Musculus*) Balb/C**

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**Abstrak**

Blood sugar is a metabolic disorder disease that occurs due to insufficiency of insulin hormone production or due to insulin insensitivity resulting in typical clinical manifestations in the form of increased glucose levels in the blood (hyperglycemia). This study aims to determine the effect of Chinese ketepeng leaf decoction on blood glucose levels in hyperglycemic mice. This research was carried out in the Zoology laboratory, Faculty of Mathematics and Natural Sciences, Pattimura University, Ambon. This research is an experimental laboratory with a pre and posttest research design with a control group design. This study wanted to prove whether there was an effect of giving Chinese ketepeng leaf decoction to decreasing blood sugar levels in male Balb/C mice using Chinese ketepeng leaf decoction at a dose of 3.64 mg/kg, 7.28 mg/kg, 10.92 mg/kg. The results showed that the administration of Chinese ketepeng leaves (Cassia alata L) can reduce blood sugar levels in mice (Mus musculus). The most effective dose to lower blood sugar levels is a dose of 10.92 mg/kg BB.

*Keywords: Diabetes mellitus (DM), Chinese ketepeng (Cassia alata* L*)*

**Introduction**

Diabetes mellitus (DM) is a metabolic disorder that occurs due to insufficiency of insulin hormone production or due to insulin insensitivity resulting in typical clinical manifestations in the form of increased blood glucose levels (hyperglycemia) (Dipiro et al., 2008). In 2017 there were 425 million people with diabetes mellitus in the world and it is estimated that this number will continue to increase until it reaches 629 million sufferers in 2045 (International Diabetes Federation, 2017).

DM is a collection of various syndromes characterized by increased blood sugar levels (hyperglycemia), changes in fat, carbohydrate and protein metabolism and an increased risk of complications of cardiovascular disease (Arokiyaraj et al, 2011). DM is a degenerative disease that continues to increase in number in Indonesia and is a disease that is spread throughout the world as a result of an unbalanced nutritional state. The prevalence and incidence of Type II DM continues to increase in both developed and developing countries (Kaempe et al, 2013).

In addition to the increasing number of sufferers, the currently available synthetic anti-diabetic drugs are quite expensive, coupled with DM treatment which requires long-term therapy. This of course will burden the patient from an economic point of view. Therefore, many people are currently paying attention to herbal therapy as a companion therapy for the treatment of DM. The World Health Organization (WHO) diabetes commission recommends further research on the use of traditional medicine as a DM therapy. Plants with hypoglycemic effects can provide a useful source for new oral antidiabetic components (Ogundipe et al., 2003).

This situation is supported by natural conditions in Indonesia. Indonesia itself is listed as the world's first mega-biodiversity country when its terrestrial and marine biodiversity is accumulated (Chan et al, 2007).

The plant (Cassia alata L) or also called Chinese ketepeng is traditionally used to treat gastrointestinal disorders, skin diseases, allergic reactions, internal and external infections and inflammatory conditions. This plant is also one of the most popular herbal medicines in natural anti-diabetic medicine in Africa (Varghese et al., 2013).

Rahmawati (2015) stated that the methanol extract of ketepeng cina leaves contains steroid compounds, flavonoids, alkaloids, saponins, and tannins. The class of flavonoids contained in Chinese ketepeng leaves is kaemferol. The mechanism of flavonoids as antidiabetics is thought to play a significant role in increasing the activity of antioxidant enzymes which can reduce oxidative stress and reduce reactive oxygen species (ROS) so that they can have a protective effect on pancreatic β cells and increase insulin sensitivity (Kaneto et al., 1999). Flavonoids contained in plants can also improve insulin receptor sensitivity and stimulate Ca2+ uptake (Shandar et al., 2011)

Researchers will conduct a blood glucose reduction test on streptozocyn-induced Balb/C male white mice using Chinese ketepeng leaves based on the literature study that has been conducted. Diabetogenic substances such as alloxan are selectively destructive to pancreatic β cells, causing depolarization of pancreatic β cells. Next, blood glucose levels will be measured using the GOD-PAP (glucose oxidase phenol 4-aminophenazone) enzymatic method.

**Method**

This research is an experimental laboratory with a pre and posttest research design with a control group design. This study wanted to prove whether there was an effect of giving Chinese ketepeng leaf decoction to decreasing blood sugar levels in Balb/C male mice.

In this study, three dose levels were made, with the conversion results from humans and mice (Mus musculus) as follows:

1). 70/50 x 0,0026 x 10% = 3,64 mg/g BB

2). 70/50 x 0,0026 x 20% = 7,28 mg/g BB

3). 70/50 x 0,0026 x 30% = 10,92 mg/g BB

After obtaining data from measuring blood sugar levels, then the data was analyzed using One Way ANOVA with a significance level of 95% to find out more about the level of difference between groups, the Duncan test was carried out. In the above analysis, homogeneity and normality tests were carried out.

**Results and Discussion**

After analyzing the normality test, homogeneity test, Anova test and Duncan test, the results of the normality test for the average blood sugar level show that there is no deviation from the normality of the blood sugar level data at a significant level (α > 0.05).

Test results for blood sugar levels in mice (Mus musculus) Balb/C induced by streptozotocin after being given Chinese ketepeng (Cassia alata L) boiled water showed that there was a decrease in blood sugar levels. The test results can be seen in Table 1.

Table 1. Average ± SD Blood Sugar Levels after administration of Chinese ketepeng (Cassia alata L) boiled water in Mice (Mus musculus)

|  |  |
| --- | --- |
| **Treatment** | **Mean ± SD Blood Sugar Level (mg/dL)** |
| Control (-) | 105,6667±12,0138a |
| Control (+) | 174,33±17,61628 c |
| Dosage 3.64 mg/kgBB | 128,33±5,85947b |
| Dosage 7.28 mg/kgBB | 118,33±1,52753b |
| Dosage 10.92 mg/kgBB | 104,6667±27,86823a |

In the positive control there was a difference with the treatment dose of 3.64 mg/kg, dose of 7.28 mg/kg, and dose of 10.92 mg/kg, while the treatment dose of 3.64 mg/kg had no difference with a dose of 7.28 mg/kg. This is due to the results of the average blood sugar levels and the Standard Deviation in the Duncan test in the treatment group with a dose of 3.64 mg/kgBW and the treatment group with a dose of 7.28 mg/kgBW showed no difference.

Table 1 shows the average blood sugar level in the negative group, the average blood sugar level is 105.6667 mg/dl. This value is used as a reference to see the difference in each treatment because the negative control was not treated. In the positive control, the average blood sugar level was 174.33 mg/dl. This value is greater than the negative control. In the positive group, mice (Mus musculus) were induced by streptozotocin so that it could cause a high average blood sugar level.

At a dose of 3.64 mg/kg, the average blood sugar level was 128.33 mg/dl. When compared with the positive control, the average value of blood sugar levels is still high. At a dose of 7.28 mg/kgBW, the average blood sugar level was 118.33 mg/dl and experienced a significant decrease when compared to the positive control and at a dose of 3.64 mg/kgBW. The results of blood sugar levels at a dose of 10.92 mg/kgBB is a dose that has an average value of blood sugar levels of 104.6667mg/dl which indicates that at a dose of 10.92mg/kgBW it can inhibit glucose transport in the blood and stimulate insulin secretion in pancreatic beta cells a significant decrease in blood sugar levels when compared to the negative control group which is in normal condition (no treatment).

Diabetes Mellitus is a condition that causes glucose levels in the blood to increase or a condition in which there is a chronic disorder characterized by hyperglycemia (increased blood glucose) and specifically involves the metabolism of carbohydrates (glucose) in the body. The results of this study indicate that the average blood sugar level in mice (Mus musculus) induced by streptozotocin after being given Chinese ketepeng (Cassia alata L) boiled water at a dose of 10.92 mg/kg BW contains flavonoids, saponins and tannins which can lower blood glucose levels. with high doses so that blood sugar levels decreased, namely the average blood sugar level was 104.67 mg/dL with a standard deviation of 9.074, when compared to the group of mice (Mus musculus) which were induced by streptozotocin after being treated with Chinese ketepeng stew at a dose of 3.64 mg/kkBB and dose of 7.28 mg/kgBB.

The decrease in blood sugar levels in mice (Mus musculus) induced by streptozotocin after being given Chinese ketepeng (Cassia alata L) boiled water at a dose of 10.92 mg/kgBW was lower. high so that the ability to inhibit α-glucosidase. The results showed that there was a decrease in blood sugar levels in mice (Mus musculus) induced by streptozotocin which were given ketepeng cina (Cassia alata L) boiled water at a dose of 10.92 mg/kgBW, 3.64 mg/kkBW and a dose of 7.28 mg/kgBW, so that it can be said that the decrease in blood sugar levels was in line with the increase in the dose of ketepeng cina (Cassia alata L) cooking water.

According to the assumptions of researchers, the content of flavonoids, saponins and tannins in Chinese ketepeng leaves (Cassia alata L) is thought to play a significant role in reducing blood sugar levels. Flavonoids, saponins and tannins in ketepeng cina (Cassia alata L) are able to overcome the effect of streptozotocin on the pancreas.

Flavonoids reduce blood glucose levels by increasing insulin secretion and insulin mimetic agents, besides that the ability of flavonoids as antioxidants can reduce oxidative stress and reduce ROS. Flavonoids, especially quercetin, are strong inhibitors of GLUT-2 absorption. This inhibition mechanism is non-competitive. This causes a reduction in the absorption of glucose and fructose from the intestine so that blood glucose levels fall. In addition, flavonoids also inhibit α-glucosidase in the intestine (Jian Song et al, 2002; Goutam, 2011).

Tannins work as a free radical scavenger by activating anti-oxidant enzymes. In addition, tannins slow down the digestion of carbohydrates by forming chelates with nutrients and together with flavonoids inhibit the digestive enzymes of glucose, namely α-amylase and α-glucosidase. In addition, tannins also stimulate an increase in glucose transport, which works similarly to insulin and stimulates the phosphorylation of the protein factor Insulin-mediated glucose transport pathway (Kumari, 2012; Xueqing Liu et al., 2005).

Saponins work to modulate calcium in pancreatic β-cells and slightly inhibit adrenaline and calcium channel blockers so that they can restore atrophic β-pancreatic cells and increase endogenous insulin production and its levels in plasma. Saponins also reduce hyperglycemia levels by restoring insulin response and sensitivity (Koneri, 2014; Zheng.et al, 2012; Elekofehinti, 2013; Kwon, 2012; Denga, 2012; Bhavsar, 2009).

Saponins also work to inhibit ROS by forming chelates with metals that cause free radicals non-enzymatically. This happens because saponins which have many -OH chains play a role in increasing antioxidant activity and the formation of free radicals. Enzymatically, saponins induce antioxidant catalysts and superoxide dismutase (SOD), which in diabetic rats the amount decreases or is very small. (Elekofehinti, 2013).

Saponins have antidiabetic activity by working to modulate calcium in pancreatic β-cells and slightly inhibit adrenaline and calcium channel blockers so that they can restore atrophic β-pancreatic cells and increase endogenous insulin production and increase hepatic glycogen and reduce the possibility of hyperinsulinemia. In addition, saponins also work to inhibit ROS and reduce levels of hyperglycemia by: restoring insulin response and sensitivity, increasing insulin levels in plasma, inducing insulin secretion in the pancreas, inhibiting disaccharide enzymes, increasing glycogen synthesis, reducing gluconeogenesis, inhibiting glucosidase, inhibiting mRNA glycogen phosphorylase and glucose 6 phosphatase, increases Glut4 expression (Koneri, 2014; Zheng.et al, 2012; Elekofehinti, 2013; Kwon, 2012; Deng, 2012; Bhavsar, 2009).

**Conclusion**

Based on the research results obtained, it can be concluded that: Administration of Chinese ketepeng leaves (Cassia alata L) can reduce blood sugar levels in mice (Mus musculus). The most effective dose to lower blood sugar levels is a dose of 10.92 mg/kg BW.

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