

*Literatur Review*

## The Effect of Pare (*Momordica Charantia* L.) Fruit Extract Fraction on Reducing Blood Sugar, Insulin Resistance and Phosphatidyl Inositol 3 Kinase (PI3K) Signalling in Male Rats (*Rattus novergicus*) Streptozotocin-induced Hyperglycemia

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### Abstract

**Background:** Diabetes mellitus (DM) is a metabolic disease characterized by symptoms of hyperglycemia as a result of impaired insulin secretion. The main cause of type 2 diabetes mellitus is a metabolic disorder characterized by insulin receptor resistance, reduced ability of pancreatic  $\beta$ -cells to secrete insulin, and abnormal insulin secretion from cells of the pancreatic islets of Langerhans. In insulin resistance, the signaling defect in Phosphatidylinositol 3-kinase (PI3K) causes impaired glucose regulation in the body. The purpose of this study was to determine the effect of bitter melon extract (*Momordica charantia* L.) on lowering blood sugar, insulin resistance, and phosphatidylinositol 3kinase (PI3K) signaling.

**Method:** Literature review studies from related journals.

**Results:** Based on research conducted, it is known that bitter melon extract has an effect on blood sugar, insulin resistance, and PI3K signaling.

**Conclusion:** Bitter melon extract has potential as an herbal antidiuretic drug.

**Keywords:** Insulin Resistance, Phosphoinositide 3-Kinase

## INTRODUCTION

Diabetes mellitus (DM) is a metabolic disease characterized by symptoms of hyperglycemia as a result of impaired insulin secretion. Impaired function of pancreatic beta cells and insulin resistance occurs as a result of obesity and related metabolic disorders.[1]

The insulin hormone functions to utilize glucose as an energy source and synthesize fat, the occurrence of insulin deficiency is caused by the pancreas no longer being able to secrete insulin.[2]

The most common type of diabetes mellitus is type 2 diabetes mellitus. The main cause of type 2 diabetes mellitus is a metabolic disorder characterized by insulin receptor resistance, reduced ability of pancreatic -cells to secrete insulin, and abnormal insulin secretion from cells of the pancreatic islets of Langerhans. The occurrence of insulin resistance in peripheral tissues which usually occurs in patients with type 2 diabetes mellitus causes most of the glucose to fail to be brought into the cells so that blood glucose levels become high. Insulin resistance initiates a state of hyperglycemia in people with type 2 diabetes mellitus.[3]

PI3Ks play an important role in glucose regulation, and this suggests

their possible involvement in the onset of diabetes mellitus. This protein acts as a key molecule of glucose homeostasis and dysregulation of its function, and thus may be involved in the elevation of serum glucose levels, which is the most important pathophysiology of diabetes. PI3K activation is the result of a direct interaction formed with the main insulin effectors, namely IRS1 and IRS2. Inhibition of PI3K blocks translocation of transporters such as Glucose transporter type 4 (GLUT-4) in insulin-stimulated cell cultures. Inhibition of PI3K decreases glucose uptake, which mainly occurs via GLUT-4, in adipocytes and other cell types.[4]. For this reason, the PI3K protein is important in insulin-mediated glucose regulation.

A high-fat diet can cause degenerative and metabolic diseases, one example is type 2 diabetes mellitus. Excessive consumption of fat that has exceeded standard requirements for a long period can cause oxidative stress due to an increase in Reactive Oxygen Species (ROS) in various tissues.[5] Treatments for people with diabetes mellitus have been found, both synthetic and natural. The use of chemical-based synthetic drugs is most often used, but the use of these drugs is long-term so

that gradually it will cause side effects and tolerance. For this reason, efforts are made to use herbal medicines from plants that have the same potential as synthetic antidiabetic drugs which are expected to have milder side effects.

Indonesia is a tropical country and has various types of plants that can be used as herbal medicines, one of which is bitter melon (*Momordica charantia*L.). Bitter melon or bitter melon is rich in the vegetable minerals calcium and phosphorus, as well as carotenoids. Bitter melon contains -momorchorin, -momorchorin and Momordica Antiviral Protein 30 (MAP30) which function as anti-HIV/AIDS. Bitter melon seeds contain triterpenoids which have anti-spermatozoa activity, so the traditional use of bitter melon seeds to prevent AIDS can cause infertility in men. Consuming bitter melon for a long time in the form of juice or vegetables can weaken and kill sperm, trigger impotence, damage the scrotum and disrupt male hormones, and even potentially damage the liver. Consumption of bitter melon for pregnant women should be limited because experiments on rats with bitter melon juice caused the miscarriage. [6]

## RESULT

Apart from being a contraceptive, bitter melon is known to regenerate damaged pancreatic beta cells. Alloxan-induced mice showed damage to pancreatic beta cells, this caused the mice to experience hyperglycemia which is an early symptom of diabetes mellitus.[7]

The content of bitter melon fruit that is useful for lowering blood glucose is insulin, lectins, charantins, and polypeptide-P. Bitter melon from the charantia and muricata varieties can empirically reduce blood glucose in diabetic test animals.[1] The content of saponins, flavonoids, polyphenols, and vitamin C in bitter melon can be used as antioxidants, which function to ward off free radicals that can interfere with the survival of Leydig cells due to diabetes mellitus. [2]

## METHODS

Research with literature review method. The literature review is research that examines or reviews several kinds of literature related to certain topics, the methods used to collect data, or sources related to topics obtained from various sources such as journals, books, the internet, and other libraries.

Based on literature studies from several related journals, it was found

that the bitter melon fruit fraction (*Momordica charantia* L.) was able to reduce blood glucose levels. The decrease in blood glucose levels is expected to prevent insulin resistance and P13K inhibition. Obtained by giving the ethyl acetate and ethanol fraction of bitter melon extract was able to reduce blood glucose levels of diabetic rats after the first week of treatment. While the n-hexane fraction was able to reduce blood glucose levels from the first day of treatment. The average bitter melon extract fraction can reduce blood glucose levels in the second week of treatment.

## DISCUSSION

### Bitter gourd Fraction Extract Against Blood Sugar Decrease

The ethanol fraction of bitter melon extract contains antioxidants in the form of flavonoids and polyphenols that can repair the cells that make up the islets of Langerhans and can lower blood glucose levels. Based on research conducted by Parawansah et al. (2020), it is known that the ethyl acetate fraction of bitter melon fruit extract 400mg/kg can reduce blood glucose levels in diabetic rats after the 4th day of treatment. Meanwhile, the n-hexane fraction of bitter melon extract decreased blood glucose levels significantly since the first day of administration. The percentage decrease in blood glucose

levels in the positive group was 69.65%. When compared with the treatment group, the highest percentage reduction in blood glucose levels h7 was found in the n-hexane fraction group of bitter melon extract of 70.95%, group of ethanol fraction of bitter melon extract of 47.84%, and a group of ethyl acetate fraction of bitter melon extract of 62,87%, While on h4 the ethyl acetate fraction group there was no decrease in blood glucose levels. [8]

Based on research by Suartha et al (2016), Decreased blood glucose levels began to be seen after four days of administration of ethanol extract of bitter melon and n-hexane fraction of bitter melon. The administration of fraction 1 and fraction 5 showed a very significant decrease ( $P>0.01$ ). And after 11 days of the administration, it was found that blood glucose levels in the administration of bitter melon ethanol extract and fraction 1 showed a normal range. The dose of 100mg/kg BW showed the best effect in lowering blood glucose levels. [9]

Research conducted by Ananta et al (2016) reported that partition of ethyl acetate of bitter melon affects the decrease in blood glucose levels of white rats (*Rattus novvergicus*) with diabetes mellitus. The ethyl acetate fraction can reduce blood glucose levels at a dose of 50 mg/kg body weight. [10]

### **Bitter gourd Fraction Extract Against Insulin Resistance and Phosphatidylinositol 3Kinase (PI3K)**

PI3K is highly involved in the regulation of glucose uptake and utilization by cells. So that if there is a disturbance in PI3K it can cause impaired blood glucose regulation and eventually can cause insulin resistance. Research by Shih et al. (2009), showed that bitter melon was effective in ameliorating dietary fructose-induced hyperglycemia, hyperleptinemia, hyperinsulinemia, and hypertriglyceridemia as well as in reducing free fatty acid (FFA) levels ( $P < 0.001$ ,  $P < 0.05$ ,  $P < 0.05$ ,  $P < 0.05$ ,  $P < 0.05$ , respectively). Bitter gourd reversed/restored dietary fructose hypoadiponectinemia ( $P < 0.05$ ), which provides a therapeutic advantage for insulin resistance in improving insulin sensitivity. [11]

While insulin's main role is the regulation of glucose levels in the blood, glucose levels can in turn regulate insulin production through negative feedback. PI3K also participates in this regulatory mechanism. In fact, PI3K inhibitors prevent insulin gene transcription in response to high glucose concentrations in pancreatic beta cells. The proliferation and growth of pancreatic beta cells similarly stimulated by PI3K, both class I isoform PI3K and class II isoform PI3K-C2 $\beta$  are

both important in the control of insulin secretion from the pancreas. [4]

Bitter melon extract fraction can significantly reduce blood sugar levels and the results are similar to the administration of synthetic drugs (Glibenclamide) in the second week of treatment. The n-hexane fraction treatment was more effective than the ethyl acetate and ethanol fractions.

### **CONCLUSION**

By the background of the problem and the purpose of the literature review from several journals, it can be concluded that there is a significant relationship between pare and hyperglycemic, where from several studies that have been previously described the hyperglycemic effect of Pare.

### **CONFLICT OF INTEREST**

The author declares that there is no conflict of interest in this study.

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