

Literature Review

Potential of Cat's Whisker (*Orthosiphon stamineus* B) As Antidiabetic in Traditional Medicine of The Dayak Tribe in West Kalimantan : A Literature Review

Sari Andayani ¹, Dianelita Asyifa Qisthi ¹, Candra Aurelion ¹, Galih Abisatya Hartono Putra ¹, Taufiq Mochammad ¹, Mistika Zakiah ², Syarifah Nurul Yanti Rizki Syahab Assegaf²

¹ Faculty of Medicine, Tanjungpura University Pontianak, West Kalimantan, Indonesia

² Department of Pharmacology, Faculty of Medicine, Tanjungpura University Pontianak, West Kalimantan, Indonesia

Corresponding Author:

Name: Galih Abisatya Hartono Putra

Email: i1011211038@student.untan.ac.id

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ABSTRACT

Introduction: Diabetes mellitus or better known as diabetes is a disease characterized by the body's inability to produce insulin or the inability to use insulin (insulin resistance). The high prevalence of diabetes sufferers in Indonesia requires attention and treatment, especially through medication. One of Indonesia's advantages compared to other countries is the biodiversity and cultural diversity sector in Indonesia, namely medicinal plants. The cat's whisker plant (*Orthosiphon stamineus* B) can be an alternative treatment for treating complications of diabetes mellitus. Cat's whisker leaves contain orthosiphon glucose, saponins, essential oils, flavonoids, polyphenols, potassium salts and myoinositol, several substances contained in this plant have the potential to lower blood sugar levels. **Methods:** This writing is a literature review by collecting literature from English and Indonesian language articles from 2014-2024, most of which are research articles. **Results:** Relevant keywords were applied in this study, which led to the selection of five scientific articles for inclusion. **Conclusion:** This research reveals that cat's whiskers (*Orthosiphon stamineus* B) show potential as an effective antidiabetic agent.

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Treatment with Orthosiphon stamineus B extract significantly reduced blood glucose levels, increased insulin secretion, and increased ghrelin and GLP-1 levels, all of which contribute to glucose regulation.

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1. INTRODUCTION

Diabetes mellitus or better known as diabetes is a disease characterized by the body's inability to produce insulin or the inability to use insulin (insulin resistance).^[1] Diabetes is classified into 2 types, namely type 1 diabetes mellitus which is influenced by hereditary factors. by an autoimmune reaction against pancreatic islet cell proteins. Type 2 diabetes is caused by a combination of genetic factors and an unhealthy lifestyle such as obesity, overeating, not eating enough, lack of exercise and stress.^[2] Diabetes is known as the "Mother of Disease" because diabetes is the parent of various diseases. others such as heart disease, hypertension, blood vessels, kidney failure and stroke.^[3] Based studi Muliani, stated that Indonesia is the fourth country in the world with the most people with diabetes. However, in 2030 Indonesia is predicted to experience an increase in diabetes sufferers by 2-3 times.^[4]

The high prevalence of diabetes sufferers in Indonesia requires attention and treatment, especially through medication. One of Indonesia's advantages compared to other countries is the biodiversity and cultural diversity sector in Indonesia, namely medicinal plants. Medicinal plants are all types of plants that have properties in helping maintain health or treating disease. These medicinal plants usually consist of ingredients originating from plants, animals, minerals, extract preparations (galenic) or mixtures of these materials that have been preserved for generations.^[5] The parts of plants that can be used consist of roots, stems, leaves, tubers or other uses. of all plants.^[6] One of the provinces in Indonesia that uses many plants as medicine is the Dayak tribe in West Kalimantan. The medicinal plant used is cat's whisker leaves (*Orthosiphon stamineus* B) as a medicine for diabetes.

The cat's whisker plant (*Orthosiphon stamineus* B) can be used as an alternative for treating diabetes mellitus.^[7] The part of the cat's whisker plant that is often used is the leaves because they contain orthosiphon glucose compounds, saponins, essential oils, flavonoids, polyphenols, potassium salts and myoinositol which have the potential to lower blood sugar levels.^[7] Testing 50% ethanol extract of cat's whiskers (*Orthosiphon stamineus* B) was proven to inhibit the enzymes α -glucosidase and α -amylase. α glucosidase inhibition has potential as an effective therapy for postprandial hyperglycemia associated with type 2 diabetes.^[8]

2. METHODS

The search used the search engines PubMed, ScienceDirect, and Google Scholar with the keywords: *Orthosiphon stamineus* B, kumis kucing, diabetes, and ethnomedicine and then screening was carried out to find articles that met the inclusion criteria. The inclusion criteria used were as follows: national and international journal articles discussing *Orthosiphon stamineus* B (kumis kucing) as an antidiabetic agent, full-text articles within the 2014-2024 range, and articles in English or Indonesian. The

exclusion criteria were articles published before 2014, articles that do not address the antidiabetic activity of *Orthosiphon stamineus B*, non-full-text articles, or review articles.

3. RESULTS

The results of searches conducted using PubMed, ScienceDirect, and Google Scholar produced 5 articles that met the inclusion and exclusion criteria. The results of the 5 articles are detailed in Table 1.

Table 1. Results of the effectiveness of *Orthosiphon stamineus B* in providing antidiabetic effects

Writer	Parts used	Research Methods	Result
Rao, et al (2014) ^[9]	Root	In Vivo	<p>Short Term Effects of Methanol Extract of <i>Orthosiphon stamineus B</i> Roots on Blood Glucose Levels in Mice</p> <p>Treatment with a single dose of <i>Orthosiphon stamineus B</i> extract showed a significant reduction in blood glucose levels compared to diabetic controls ($P < 0.01$). The effect produced by a dose of 800 mg/kg was comparable to the effect of glibenclamide ($P < 0.01$).</p> <p>Long Term Effects of Methanol Extract of <i>Orthosiphon stamineus B</i> Roots on Blood Glucose Levels in Mice</p> <p>In a long-term study, administration of methanolic extract of <i>Orthosiphon stamineus B</i> roots for four weeks significantly reduced fasting blood glucose levels in streptozotocin (STZ)-injected mice compared with diabetic controls ($P < 0.01$). A significant decrease occurred after one week of administration. The glucose lowering effect was dose dependent, with a dose of 400 mg/kg showing a comparable effect to glibenclamide ($P < 0.01$), while a dose of 800 mg/kg had a greater effect than glibenclamide (600 µg/kg) ($P < 0.05$). However, administering the extract at doses of 200 mg/kg, 400 mg/kg, and 800 mg/kg did not show significant changes in serum insulin levels compared to diabetic controls.</p>
Lee, et al (2015) ^[10]	Leaf	In vitro	<p>a) Crude <i>Orthosiphon stamineus B</i> (OS) extract increased insulin mRNA expression in INS-1 cells in both normal and hyperglycemic (HG) conditions. In addition, the hexane and ethylacetate fractions of OS extract also increased insulin mRNA expression in INS-1 cells under both conditions. In contrast, the water and butanol fractions of OS did not affect insulin mRNA expression. The hexane fraction of OS increased insulin and PDX-1 mRNA levels in INS-1 cells in a dose-dependent manner.</p>

			<p>b) After three days in HG conditions, glucose-stimulated insulin secretion is completely inhibited (glucotoxicity in INS-1 cells). OS hexane extract concentration of 200 μM protected INS-1 cells from this glucotoxicity.</p> <p>c) OS hexane extract increased p-PI3K levels in a dose-dependent manner. Akt phosphorylation was also increased by treatment with 100 and 200 μmol of OS extract.</p> <p>d) HG increased peroxide concentration in INS-1 cells, but treatment with OS extract did not affect peroxide levels in either normal or HG conditions.</p>
Masrif, et al (2015) ^[11]	Leaf	Experimental (pre- & post- test design)	<p>The treatment group given cat's whisker leaf capsules at a dose of 0.75 grams was effective in reducing blood glucose levels during administration for 7 days. It can be seen based on the following results:</p> <p>a) The blood glucose level before for the treatment group was 148.45 ± 19.77 while for the group without treatment it was 148.39 ± 12.60.</p> <p>b) The average difference in blood glucose levels after administration of cat's whisker leaf capsules for the treatment group was 89.61 ± 17.92, while for the group without treatment it was 104.23 ± 12.59.</p> <p>c) The difference for the treatment group is larger, namely 58.84, with the difference without treatment being smaller, namely 44.16.</p>
Lokman, et al. (2019) ^[12]	Leaf	In vitro & In vivo	<p>In vitro studies:</p> <p>a) At low glucose it doesn't have much of an effect without insulin stimulation. At high glucose Orthosiphon stamineus B provided insulin release increased by 7.7, 30.3 and 102.4 times.</p> <p>In vivo studies:</p> <p>a) Non-pregnant mice were given Orthosiphon stamineus B food amounting to 358 ± 20.7 g. Pregnant mice were fed at 267.7 ± 3 g. There was no significant difference in body weight changes between different groups in non-pregnant and pregnant mice.</p> <p>b) Giving an oral glucose tolerance test to the non-pregnant group gave significant results. Blood glucose and insulin levels showed a low curve indicating a significant difference in response to 2 weeks of treatment with Orthosiphon stamineus B compared to control diabetic mice. The results of experiments on</p>

			pregnant diabetic mice with daily intake of Orthosiphon stamineus B for 10 days gave the same results with low blood glucose and insulin levels.
Bassalat, et al (2023) ^[13]	Aerial parts	In vitro & In vivo	<p>Effect of Orthosiphon stamineus B Extract on Blood Sugar Levels of Mice (observed on day 36)</p> <p>a) Diabetic mice without treatment: 359 ± 7 mg/dL</p> <p>b) Diabetic mice treated with Orthosiphon stamineus B methanol extract: 174 ± 3 mg/dL</p> <p>c) Diabetic mice treated with Orthosiphon stamineus B distilled water extract: 164 ± 2 mg/dL</p> <p>d) Non-diabetic mice both treated and untreated: 104 mg/dL - 109 mg/dL</p> <p>Overall, Orthosiphon stamineus B aqueous extract and Orthosiphon stamineus B methanol extract can reduce blood sugar levels by 54% and 57%, respectively.</p> <p>Phytochemical screening results of Orthosiphon stamineus B extract</p> <p>a) Orthosiphon stamineus B aqueous extract: contains 52 compounds (4 compounds are suspected to be antidiabetic)</p> <p>b) Orthosiphon stamineus B methanol extract: contains 41 compounds (6 compounds are suspected to be antidiabetic)</p> <p>Effect of Orthosiphon stamineus B extract on GLUT-4 Translocation</p> <p>a) Orthosiphon stamineus B distilled water extract:</p> <ol style="list-style-type: none"> 250 µg/mL: 100% to 142 ± 2.5% and 165 ± 5% with and without insulin, respectively <p>b) Orthosiphon stamineus B methanol extract:</p> <ol style="list-style-type: none"> 250 µg/mL: 100% to 279 ± 15% and 351 ± 20% without and with insulin, respectively

4. DISCUSSIONS

4.1 DIABETES

Type 2 diabetes is a metabolic disease characterized by chronic hyperglycemia due to insulin resistance, impaired insulin secretion, or both. The causes of type 2 diabetes are multifactorial, including genetic, environmental and lifestyle factors. The main risk factors include obesity, lack of physical activity, a high-calorie diet, and genetic predisposition. Certain genetic mutations can disrupt pancreatic beta cell function or insulin signaling, contributing to the development of type 2 diabetes. Insulin resistance is a key feature in the pathophysiology of type 2 diabetes, where the body becomes less responsive to the action of insulin, a hormone that plays an important role in glucose

metabolism. Insulin normally works by binding to insulin receptors on the surface of cells, which triggers a series of intracellular signals to get glucose from the blood into cells, especially in muscle, adipose and liver tissue. In insulin resistance, this signaling pathway is disrupted, resulting in reduced insulin effectiveness in lowering blood glucose levels.^[14]

Some of the mechanisms underlying insulin resistance involve changes in insulin receptors, disruption of intracellular signaling, and accumulation of lipids in cells. Lipid accumulation, particularly in muscle and liver, can disrupt mitochondrial function and increase oxidative stress, contributing to insulin resistance. Adipocytes (fat cells) also play an important role, because in conditions of obesity, there is an increase in the secretion of pro-inflammatory cytokines such as TNF- α and IL-6 which can inhibit insulin signals.^[14]

In response to insulin resistance, the pancreas increases insulin secretion to maintain normoglycemia. In the early stages, this condition is known as compensatory hyperinsulinemia, where high insulin levels are able to overcome insulin resistance, keeping blood glucose levels normal. However, over time, persistent stress on pancreatic beta cells leads to a decrease in the ability of these cells to produce insulin, either due to beta cell exhaustion, apoptosis, or due to glucotoxicity and lipotoxicity caused by high levels of glucose and free fatty acids.^[14]

Treatment of type 2 diabetes involves a combination of lifestyle changes and pharmacological therapy. Lifestyle modifications include a diet low in calories and fat, increased physical activity, and weight loss. Pharmacologic therapy usually begins with oral agents such as metformin, which increases insulin sensitivity and decreases glucose production by the liver. If glycemic control is not achieved, other medications such as sulfonylureas, DPP-4 inhibitors, or GLP-1 agonists may be added. In advanced stages, exogenous insulin may be necessary. Control of cardiovascular risk factors such as hypertension and dyslipidemia is also important in the management of type 2 diabetes to prevent long-term complications.^[14]

4.2 Orthosiphon stamineus B

Orthosiphon stamineus B, commonly known as cat's mustache and cat's whiskers, is a native plant from Bangladesh, Bismarck Islands, Kalimantan, Cambodia, South-Central China, Southeast China, Hainan, India, Java, Laos, Lesser Sunda Islands, Malaya, Maluku, Myanmar, New Guinea, Philippines, Queensland, Sri Lanka, Sulawesi, Sumatra, Taiwan, Thailand and Vietnam. The cat's whisker plant is also distributed in several other countries, including the Caroline Islands, Fiji and Niue. This plant has the following taxonomy:^[15]

Table 2. Taxonomy *Orthosiphon stamineus* B

Kingdom	: Plantae
Division	: Magnoliophyta
Class	: Magnoliopsida
Ordo	: Lamiales
Family	: Lamiaceae
Genus	: <i>Orthosiphon</i>
Species	: <i>Orthosiphon stamineus</i> B.

This plant is a perennial plant that can grow to a height of around 1 meter. This plant needs full sunlight and moist soil to grow well. Cat's whisker plants can grow in shady conditions, but not in places that are too shady and warm. *Orthosiphon stamineus* B has two varieties based on flower color, a white variety and a purple variety. Some also categorize them into purple, intermediate and white varieties (Figure 2). The purple variety of cat's whiskers has a higher bioactive ingredient composition than the white variety. As many as 69% of *Orthosiphon stamineus* B plants are white varieties. *Orthosiphon stamineus* B can grow up to 1.2 meters and the leaves can be harvested after 2-3 months after planting.^{[16][17]}

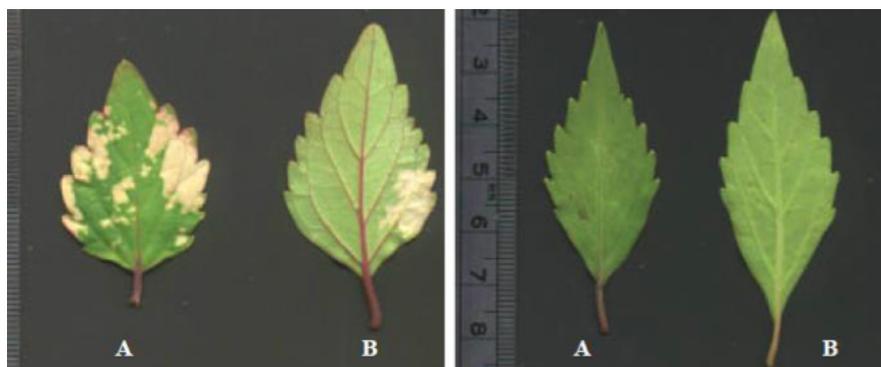


Figure 1. Morphology of *Orthosiphon stamineus* B leaves seen on the top (A) and bottom surface (B). Left: Purple Variety; Right: White Variety.

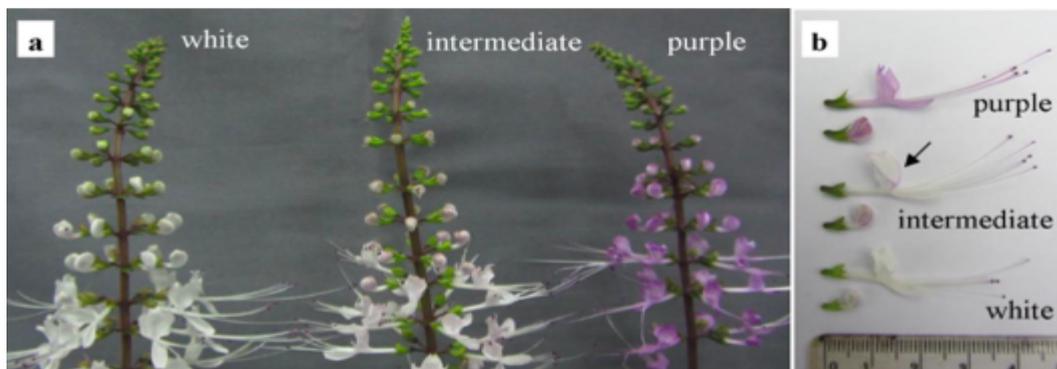


Figure 2. *Orthosiphon stamineus* B Flower

4.3 THE ROLE OF ORTHOSIPHON STAMINEUS B IN DIABETES

Orthosiphon stamineus B has biological activity which is attributed to the presence of several active compounds including rosmarinic acid, phenolics, flavonoids, amino acids and coumarin. UHPLC-ESI analysis of Orthosiphon stamineus B extract revealed the presence of 5 polyphenolic compounds such as rosmarinic acid, chlorogenic acid, caffeic acid, sinensetin, and eupatorin. Orthosiphon stamineus B shows potential as an effective antidiabetic agent. Treatment with Orthosiphon stamineus B extract significantly reduced blood glucose levels, increased insulin secretion, and increased ghrelin and GLP-1 levels, all of which contribute to glucose regulation. According to research by Lokman et al., no signs of toxicity or significant changes in body weight were found, either in pregnant or non-pregnant mice, indicating that Orthosiphon stamineus B is safe to use.^[9]

Orthosiphon stamineus B leaves contain various substances such as essential oils, flavonoids, orthosiphon glycosides, saponins, potassium salts, and myoinositol. Two important substances that play a role in reducing blood glucose levels are flavonoids and saponins. The flavonoids in cat's whiskers are able to inhibit the enzymes glucosidase and alpha-amylase, which function in breaking down carbohydrates into monosaccharides. With this inhibition, the breakdown of carbohydrates into monosaccharides does not occur, so no glucose (monosaccharides) can be absorbed by the intestines, causing a decrease in blood glucose levels.^[12]

Saponins also play a role in lowering blood glucose levels by inhibiting the Nat/D-glucose cotransport (SGLUT) system in the intestinal brush border membrane. This blocks glucose transport in the intestine, so that glucose absorption is hampered and causes a hypoglycemic effect. Orthosiphon stamineus B has two important substances, flavonoids and saponins, which contribute to lowering blood glucose levels. Flavonoids inhibit the enzymes glucosidase and alpha-amylase, while saponins inhibit the Nat/D-glucose cotransport system in the intestine. Both of these mechanisms cause a decrease in blood glucose levels.^[12]

Research conducted by Masrif, et al. (2014) in diabetes mellitus patients in the outpatient room of the Bahteramas General Hospital, Southeast Sulawesi Province, showed that administering cat's whisker powder in capsule form had a fairly good effect on reducing blood glucose. Cat's whisker capsules are given at a dose of 0.75 grams for 7 days. Testing was carried out on 62 outpatients, divided into treatment groups and non-treatment groups. The blood glucose level before for the treatment group was 148.45 ± 19.77 , while for the group without treatment it was 148.39 ± 12.60 . The average difference in blood glucose levels after administration of cat's whisker leaf capsules for the treatment group was 89.61 ± 17.92 , while for the group without treatment it was 104.23 ± 12.59 . These results indicate that the treatment group experienced a more significant reduction in blood glucose levels compared to the group without treatment. It was not explained in more detail whether there was conventional treatment given to the group without treatment so that it was not possible to compare the effectiveness of cat's whiskers with certain drugs. This study also only used one dose variation so it was not possible to determine the most effective dose formulation. This research examines a small number of samples with diverse characteristics.^[12]

Based on research by Bassalat et al., Orthosiphon stamineus B water and especially methanol extract significantly reduced the plasma glucose concentration of

streptozotocin-induced diabetic rats. Simultaneously, methanol extract was more efficient in increasing GLUT4 translocation to the plasma membrane of L6 myocytes. Among the detected compounds, 10 were reported to increase GLUT4 transport or translocation to the PM. In addition, Orthosiphon stamineus B extract showed antioxidant activity that may be related to antidiabetic activity and glucose disposal.^[10]

Based on research by Lee et al., it was found that Orthosiphon stamineus B crude extract could increase insulin mRNA expression in INS-1 cells. To identify the specific components in the Orthosiphon stamineus B extract that are responsible for the stimulation of insulin production, a fractionation process was carried out. Ethyl acetate and hexane fractions increased insulin mRNA expression under normal conditions and high glucose levels for 12 hours. However, the ethyl acetate fraction caused cell death after 3 days of cultivation with high glucose levels.^[11]

Orthosiphon stamineus B hexane extract was found to increase insulin mRNA expression and insulin secretion, while protecting β cells from glucotoxicity due to high glucose exposure. Lee In contrast, previous research by Mohamed et al. stated that the antidiabetic effect of Orthosiphon stamineus B is more related to the inhibition of glucose absorption in the intestine and the enhancement of glucose absorption by the diaphragm, rather than the stimulation of insulin secretion, which may be due to differences in experimental methods.^[18]

Orthosiphon stamineus B hexane extract activates signaling pathways involving PI3K, Akt, and PDX-1, all of which are important for insulin mRNA expression. A possible mechanism of β -cell protection is also associated with the antioxidant activity of this extract, although no antioxidant effect was found from the Orthosiphon stamineus B hexane extract. Orthosiphon stamineus B hexane extract not only increases insulin mRNA expression but also protects β cells from glucotoxicity, possibly through activation of PI3K and Akt.^[11]

The roots of Orthosiphon stamineus B also have potential as an antidiabetic agent. Research conducted by Rao, et al. showed that oral administration of methanolic extract of Orthosiphon stamineus B roots to streptozotocin (STZ)-induced type 2 diabetic rats resulted in a significant reduction in blood glucose levels. This lowering effect is dose-dependent, with a dose of 800 mg/kg showing a reduction in blood glucose levels that is comparable to glibenclamide. Additionally, administration of the extract for four weeks significantly reduced the activity of the enzyme glucose 6-phosphatase (G6P) in the liver and increased glycogen levels, indicating that the extract works through mechanisms outside the pancreas. However, serum insulin levels did not show significant changes, indicating that the antidiabetic effect of this extract was not through increasing insulin secretion.^[13]

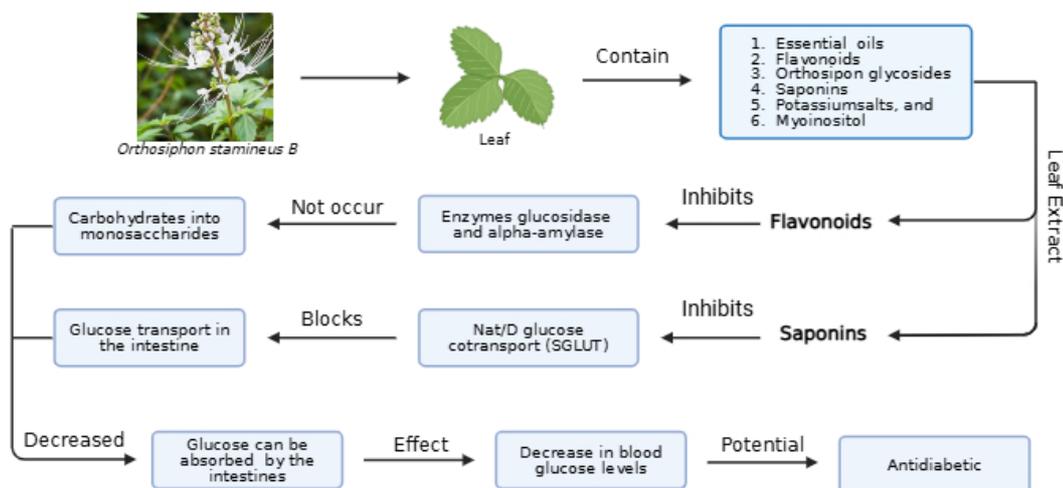


Figure 3. *Orthosiphon stamineus B* potential antidiabetic

4.4 USE OF THE *Orthosiphon Stamineus B* BY THE DAYAK ETHNIC GROUP

The cat's whisker plant is widely used by Dayak ethnic groups in West Kalimantan, especially the Tanjung Dayak tribe, Ribau Village, Kapuas District, Sanggau Regency and the Seberuang Dayak tribe in the forest area of Ensabang Village, Sepuk District, Sintang Regency. The cat's whisker plant is believed to have an antidiabetic effect because it contains flavonoid and saponin compounds which can inhibit the work of the alpha glucosidase enzyme.^[19] In the Kendawangan Dayak tribe in Rangkung Village, Marau District, Ketapang Regency, cat's whiskers are used by boiling the leaves and then drinking them straight away.^[20] Apart from being useful for diabetes, cat's whiskers are also widely used by the Dayak tribe in Ensabang village, Sintang district, to treat back pain by using parts of the roots of the cat's whisker plant. Another Dayak tribe in the village of Stock uses cat's whiskers as a medicine for more common ailments such as vaginal discharge, urinary stones and back pain. In Bengkayang district, there is another use of cat's whiskers, namely as a medicine for malaria by drinking boiled water.^[19]

5. CONCLUSION

This research reveals that cat's whiskers (*Orthosiphon stamineus B*) show potential as an effective antidiabetic agent. Treatment with (*Orthosiphon stamineus B*) extract significantly reduced blood glucose levels, increased insulin secretion, and increased ghrelin and GLP-1 levels, all of which contribute to glucose regulation. The cat's whisker plant is believed to have an antidiabetic effect because it contains flavonoid and saponin compounds which can inhibit the work of the alpha glucosidase enzyme. Therefore, the cat's whisker plant is used by many Dayak ethnic groups in West Kalimantan. Further research regarding the antidiabetic potential of the cat's whisker plant needs to be carried out to determine its pharmacological effects, benefits, dosage and toxicity for humans.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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