GSC Biological and Pharmaceutical Sciences

eISSN: 2581-3250 CODEN (USA): GBPSC2

Cross Ref DOI: 10.30574/gscbps

Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

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Evaluation of blood glucose lowering activity of Coffea robusta leaf extract in mice induced by alloxan

Rudi Kartika *, Bohari, Subur P. Pasaribu, Aman Sentosa Panggabean, Daniel and Dirgarini Julia Nurlianti

Department of Chemistry, Faculty of Mathematics and Natural Sciences, Mulawarman University, Jl. Barong Tongkok No. 4 Kampus Gn. Kelua Samarinda Telp. 0541-74915.

GSC Biological and Pharmaceutical Sciences, 2025, 31(02), 017-021

Publication history: Received on 10 February 2025; revised on 17 March 2025; accepted on 20 March 2025

Article DOI: https://doi.org/10.30574/gscbps.2025.31.2.0119

Abstract

An investigation of the antidiabetic activity of coffee leaf (Coffearobusta) extract in ethanol with doses 13,95, 27,9 and 55,8 mg/kg BW given orally to white male mice. Measurement of the blood glucose level was done day to-0, 8 and 18 using glucometer and glucotest strip. Doses variation of the ethanol extract coffee leaf showed that the dose of 27,9 mg/kg BW gave the best antidiabetic activity 59,61%. This experiment showed gave the best antidiabetic activity result gift ethanol extract coffee leaf. And Phytochemical screening ofthe ethanol extract coffee leaf showed the presence of alkaloids, phenols, saponnins, flavonoids and triterpenoids.

Keyword: Coffea leaf; Blood glucose; Mice; Alloxan

1. Introduction

The use of plants as traditional medicine is still widely practiced in Indonesia, especially in rural areas rich in plant biodiversity. Besides being affordable and easy to obtain, traditional medicines derived from plants have far fewer harmful side effects compared to synthetic drugs. To enhance the role of traditional medicine, efforts must be made to introduce, research, test, develop the efficacy, and ensure the safety of medicinal plants to eliminate misconceptions about traditional treatments [1].

Coffee plants are well-known in Indonesian society. For coffee enthusiasts, it may never occur that aside from its beans, coffee leaves can also be used as a beverage ingredient. Besides having an aroma and taste that is equally delightful, coffee leaves offer many health benefits for the body.

Historically, this practice is unique. It is said that during the Japanese occupation of the Minang region, fresh coffee beans from the land of local residents were confiscated and exported. As a result, locals could not enjoy brewed coffee, which at the time symbolized a certain level of status. Consequently, the community substituted coffee beans with coffee leaves, which turned out to have a taste not inferior to coffee beans. Since then, the tradition of drinking coffee leaf tea has been preserved. The community uses coffee leaves to treat ringworm, lower high blood pressure in hypertensive patients, warm the body, improve respiratory flow, and increase stamina and vitality.

Diabetes mellitus, commonly known as diabetes or high blood sugar, is caused by a deficiency of the insulin hormone. This occurs because the pancreas, which produces insulin, fails to produce sufficient amounts, leading to hyperglycemia. Prolonged hyperglycemia can result in fatal complications and even death. Hyperglycemia can be prevented by strictly controlling blood sugar levels [2].

* Corresponding author: Rudi Kartika

In the community, coffee leaves are used as a traditional medicine for diabetes. Secondary metabolites contained in coffee leaves include tannins, flavonoids, and polyphenols [3].

Based on the explanation above, the research problem is formulated as follows: Can the ethanol extract of Coffea robusta leaves reduce blood glucose levels in mice induced with alloxan?

The objective of this study is to determine the activity of Coffea robusta leaf extract in reducing blood glucose levels in mice induced with alloxan.

The benefit of this research is the potential use of Coffea robusta leaves as an alternative treatment for diabetes mellitus.

1.1. Tools

The tools used in this research include:

Digital scales, rotary evaporator, glucometer and glucotest strips, beaker glass, glass funnels, spatula, stirring rods, dropper pipettes, micro pipettes, Erlenmeyer flasks, maceration vessels, 25 ml volumetric flasks, 100 ml volumetric flasks, surgical scissors, spray bottles, mice cages, hot plate, volumetric pipettes, test tubes, test tube racks, knives, and blenders.

2. Materials and method

The materials used in this research include:

96% ethanol, distilled water, filter paper, cotton, alloxan, glibenclamide 0.02% (b/v), CMC-Na 1%, chloroform, ammonia solution, H2SO4(p), HCl(p), glacial acetic acid, Meyer's reagent (KI and HgCl2), Dragendorff's reagent (KI solution and bismuth nitrate), FeCl3 1% solution, magnesium powder, aluminum foil, and tissue.

The sample used in this study was the leaves of Coffea robusta plants obtained from Kaliorang, East Kalimantan. The research was conducted in the Biochemistry Laboratory, Faculty of Mathematics and Natural Sciences, Mulawarman University, Samarinda, in 2015. The coffee leaves were dried by air-drying and then ground using a blender. A total of 134 grams of dried coffee leaf powder was macerated with 96% ethanol for three days. Maceration aims to extract the active substances [2]. The extract was filtered, concentrated using a rotary evaporator, and then weighed. The research included phytochemical screening and antihyperglycemic testing.

The antihyperglycemic test was conducted using male mice aged 2–3 months, weighing 20–30 grams. Initially, the mice were divided into five groups and given the following test preparations:

- Group I (negative control) received 1% CMC.
- Group II (positive control) received 0.009 mg/20 g BW of glibenclamide.
- Groups III–V (test groups) were given ethanol extract of coffee leaves at doses of 13.95, 27.9, and 55.8 mg/kg BW, respectively.

The doses used in this study were calculated based on common human usage (15 g of dried leaves for a 50 kg body weight). According to the human-to-mice dosage conversion table for a 70 kg human, the conversion factor is 0.0026.

The experimental groups were administered alloxan at 100 mg/kg BW every four days to increase their blood glucose levels. Blood glucose levels were measured on days 0, 8, and 18. Before blood glucose measurement, the test animals were fasted for 16 hours. During fasting, husks were removed from the cages to prevent the animals from eating them. Blood glucose measurements were performed using a glucometer. On day 8, blood glucose levels were measured to evaluate the increase in blood glucose levels. Blood sampling was done from the vein in the tails of the test animals. The test preparations were administered to the test animals from day 9 to day 18.

3. Results and Discussion

From 134 grams of dried Coffea robusta leaf powder, after being macerated with 96% ethanol for 3 days, a liquid extract was obtained. Then, after the liquid extract was concentrated using a rotary evaporator, 6 grams of dry extract were produced, equivalent to 4.5% of the dried leaves.

In this experiment, blood glucose levels were measured on days 0, 8, and 18. The calculation of days began from the first administration of alloxan. Therefore, day 0 was the first day alloxan was administered. On day 4, all the test animals were re-induced with alloxan, except for the negative control group. By day 8 of the treatment, the blood glucose levels of the test animals had shown a significant increase, and for that reason, the test substances were administered from day 9 to day 18.

The fasting blood glucose levels of the test animals on days 0, 8, and 18 for each group can be seen in Table 1.

Table 1 Blood Glucose Levels of Male Mice in Response to Treatment

Treatment Groups	Blood Glucose Level (mg/dL)		
	Fasting Blood	Alloxan Administration	Extract Administration
(K-)	60	53	51
(K+)	78	217	69
D1	69	197	107
D2	58	203	82
D3	77	205	70

Alloxan provides a quick method for inducing experimental diabetes in various vertebrates. Alloxan is thought to act directly and specifically on beta cells, causing their degeneration and resorption, while alpha cells and acinar tissue remain relatively unaffected. However, animals with alloxan-induced diabetes do not entirely lose insulin [4]. Alloxan can produce highly reactive hydroxyl radicals, which can induce diabetes in experimental animals. The diabetogenic effects of alloxan can be prevented by hydroxyl radical scavenger compounds [5].

To determine the effect of coffee leaf extract on lowering fasting blood glucose levels in test animals, the percentage reduction in blood glucose levels in mice on day 18 was calculated and is presented in Table 2.

Table 2 Percentage Reduction in Blood Glucose Levels with the Administration of Glibenclamide and Coffee Leaf Extract

Treatment Groups	Increased glucose level mg/dL (Day - 4)	Reduction glucose level mg/dL (Hari ke-14)	Precentage glucose level reduction (%)
(K+)	217	69	68,20
D1	197	107	45,69
D2	203	82	59,61
D3	205	70	65,85

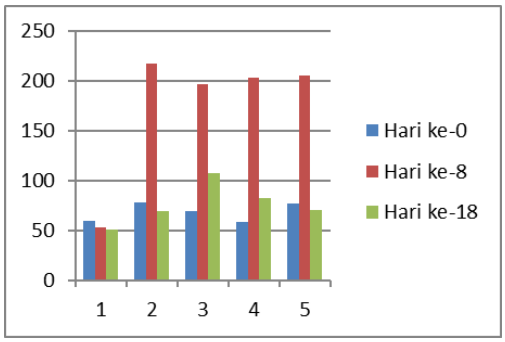

Figure 1 Graph of blood glucose levels in mice

From the graph above, the blood glucose levels in male mice after the administration of glibenclamide and coffee leaf extract at low, medium, and high doses showed a decrease in glucose levels. Glibenclamide (glyburide, Daonil, Euglucon, Renabetic) is a sulfonylurea derivative with a strong antidiabetic effect [6]. In this study, the most effective dose for reducing blood glucose levels in test animals was the medium dose (27.9 mg/Kg BW).

The ethanol extract of coffee leaves can reduce blood glucose levels in test animals at low doses (13.95 mg/Kg BW), medium doses (27.9 mg/Kg BW), and high doses (55.8 mg/Kg BW), likely due to the presence of compounds in coffee leaves, including alkaloids, saponins, triterpenoids, flavonoids, and phenolics.

Alkaloids have been proven to regenerate damaged pancreatic β-cells. The increase in insulin secretion is caused by the sympathetic nerve-stimulating effects (sympathomimetic) of alkaloids, which result in increased insulin secretion [7]. Alkaloids stimulate the hypothalamus to increase the secretion of Growth Hormone Releasing Hormone (GHRH), which leads to increased secretion of Growth Hormone (GH) from the pituitary gland. Elevated GH levels stimulate the liver to secrete Insulin-like Growth Factor-1 (IGF-1). IGF-1 has effects that induce hypoglycemia and reduce gluconeogenesis, thereby lowering blood glucose levels and insulin requirements [8]. According to [7], alkaloids reduce blood glucose by inhibiting glucose absorption in the intestines, enhancing glucose transport in the blood, stimulating glycogen synthesis, and inhibiting glucose synthesis by blocking the enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase, as well as enhancing glucose oxidation through glucose-6-phosphate dehydrogenase. Glucose-6-phosphatase and fructose-1,6-bisphosphatase are enzymes involved in gluconeogenesis. Inhibition of these enzymes reduces glucose production from non-carbohydrate substrates.

The mechanism of action of saponins in lowering blood glucose levels is through the inhibition of glucose transport in the digestive tract and stimulation of insulin secretion in pancreatic beta cells [8].

Flavonoids, through their antioxidant effects, indirectly support anti-inflammatory effects. Flavonoids can prevent diabetes mellitus complications or progression by scavenging excessive free radicals and breaking free radical chain reactions. The presence of free radicals attracts various inflammatory mediators, and flavonoids stabilize Reactive Oxygen Species (ROS) by reacting with reactive radical compounds, rendering them inactive [9].

Phenolic compounds also have antioxidant activity, which can reduce oxidative stress by preventing chain reactions that convert superoxide into hydrogen peroxide. This is achieved by donating hydrogen atoms from aromatic hydroxyl (-OH) groups to bind free radicals and removing them from the body through the excretory system [8].

4. Conclusion

Based on the results obtained, it can be concluded that coffee leaves can be used as antidiabetic therapy because they are capable of reducing blood glucose levels and repairing damage to the pancreatic islets of Langerhans, particularly at a dose of 27.9 mg/kg BW during a 10-day treatment period.

Suggestion

Research can be conducted with time variations by measuring blood glucose levels every three days to determine the range of reduction in blood glucose levels in mice.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

Ethical approval for this study was obtained from "the ethical committee of medical research of Universitas Muhammadiyah Lamongan with approval number [151/EC/KEPK-S3/04/2025]

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