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Original Research Article

Combination of purple sweet potato (*Ipomoea batatas L.*) leaf extract with metformin on blood glucose and total cholesterol levels of albino rats induced by high-fat diet and streptozotocin

Marselina Saing, Urip Harahap*, Panal Sitorus

Department of Pharmacology, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Indonesia

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***Correspondence:**
Dr. Urip Harahap,
Email: urip@usu.ac.id

ABSTRACT

Background: Diabetes mellitus is a metabolic disease characterized by hyperglycemia due to impaired insulin secretion, often accompanied by hypercholesterolemia. Metformin is a first-line antihyperglycemic drug that is often combined with other antihyperglycemic drugs. Purple sweet potato leaves have been widely studied to reduce glucose and cholesterol levels.
Methods: This study was an experimental study using rats induced with a high-fat diet and streptozotocin, which were divided into 8 treatment groups, namely groups given CMC Na 0.5%, Metformin 45 mg/kg BW, Purple Sweet Potato Leaf Extract (SPLE) 200 mg/kg BW, SPLE 400 mg/kg BW, SPLE 800 mg/kg BW, SPLE 200 mg/kg BW with metformin 45 mg/kg BW, SPLE 400 mg/kg BW with metformin 45 mg/kg BW, and SPLE 800 mg/kg BW with metformin 45 mg/kg BW.
Results: After treatment for 28 days with SPLE doses of 200 mg, 400 mg, and 800 mg/kg BW, both single doses and combinations with metformin showed a decrease in fasting blood glucose levels and total cholesterol, which were statistically significantly different ($p<0.05$) between treatment groups using the one-way ANOVA. The combination of SPLE 800 mg/kg BW with metformin normalized blood glucose levels of 93.50±4.93 mg/dl.
Conclusion: The combination of purple sweet potato leaf extract with metformin is more effective in reducing blood glucose and total cholesterol levels compared to the single administration of metformin and SPLE.

Keywords*:* Diabetes mellitus, SPLE, Metformin, Total cholesterol

INTRODUCTION

Diabetes mellitus (DM) is one of the five leading causes of death in the world.[1] The prevalence of diabetes mellitus in the world continues to increase year by year.[2] Abnormal glucose and lipid metabolism in DM patients leads to hyperlipidemia; triglycerides and cholesterol increase significantly; and HDL decreases.[3,4] Hyperglycemia and dyslipidemia are two major components of the metabolic dysregulation for type 2 DM and major risk factors for cardiovascular disease.[4] In the development of DM treatment, there is a great need for DM therapy with herbal products.[5] These herbal products are combined with conventional drugs, one of which is metformin. Metformin is the first-line antihyperglycemic drug in pharmacological therapy of type 2 DM and the most commonly prescribed drug worldwide, either as a single therapy or in combination with insulin or other glucose-lowering drugs5,6. Metformin can also reduce triglycerides and increase HDL cholesterol.[5-9]

One of the plants that has been widely studied to have the effect of lowering blood glucose levels and blood lipids is sweet potato leaves. Bioactive compounds of sweet potato leaves that are beneficial to health include phenolic acids, flavonoids, alkaloids, saponins, coumarins, and tannins. These bioactive compounds are effective as antioxidants, anticancer, antimutagenic, immunomodulators, and hepatoprotectors.[10] Purple sweet potato leaves contain the highest amount of anthocyanin, which is useful as a strong antioxidant. The aqueous extract of *Ipomoea batatas* leaves in rats induced with a high-fat diet showed weight loss, decreased levels of cholesterol, triglycerides, LDL, VLDL, and increased HDL.[11,12] The purpose of this study was to determine the difference in activity of the combination of SPLE with metformin on blood glucose and total cholesterol levels in diabetes mellitus rats induced by a high-fat diet and streptozotocin.

METHODS

This research was carried out from January to May 2023 at the Pharmacology Laboratory, Faculty of Pharmacy, Universitas Sumatera Utara, Medan, Sumatera Utara.

Preparation of sweet potato leaf simplician powder

Sweet potato leaf samples were sorted for impurities, washed thoroughly under running water, drained, and weighed. Samples were dried in a drying cabinet at a temperature of ±40°C until brittle. Simplisia that has been dried is blended into simplisia powder.

Preparation of sweet potato leaf's extract

The purple sweet potato leaves were extracted using 70% ethanol (1:4 v/v) by the maceration method. The filtrate was evaporated using a rotary evaporator at a temperature of 60°C to get a concentrated extract.

Procedure

The experimental animals used in this study were male white rats (Rattus norvegicus L.) of the Wistar strain weighing 180 to 220 grams, 8-10 weeks old, and in normal condition. Rats were acclimated for 7 days at room temperature and a 12:12 hour light/dark cycle. with standard food and drink ad libitum. Rats were induced to eat a high-fat diet (STZ). The high-fat diet was given for 4 weeks and followed by intraperitoneal administration of streptozotocin (30 mg/kg BB). After 3 days of STZ administration, the blood glucose levels of rats were checked. They were categorized as diabetic if their blood glucose levels were ≥ 200 mg/dl.[13]

Animal treatment

The sweet potato leaf extract (SPLE) was suspended in the CMC Na 1% to make it homogenous. The animals were divided into eight groups; they were randomly selected, and each group consisted of four rats. Group 1: given Na-CMC 0.5% (negative control) for 28 days; Group 2: given a metformin dose of 45 mg/kg BW (positive control) for 28 days; Group 3: given SPLE 200 mg/kg BW for 28 days; Group 4: given SPLE 400 mg/kg BW for 28 days; Group 5: given SPLE 800 mg/kg BW for 28 days; Group 6: given a combination of SPLE 200 mg/kg BW with metformin 45 mg/kg BW for 28 days; Group 7: given a combination of SPLE 400 mg/kg BW with metformin 45 mg/kg BW for 28 days and Group 8: given a combination of SPLE 800 mg/kg BW with metformin 45 mg/kg BW for 28 days.

Blood glucose levels and total cholesterol levels were measured on days 0, 7, 14, 21, and 28. Blood sampling was done after the rats were fed for 12 hours. The fasting blood glucose (FBG) measurement method was carried out enzymatically using the Easy Touch Test Strip by means of blood samples taken from the lateral vein of the tail, which was first cleaned with an alcohol swab dripped on the strip that had been paired on the tool. After 10 seconds, the blood glucose level will appear on the monitor screen of the tool.

Statistical analysis

Data obtained from all treatment groups were analyzed by the one-way ANOVA (analysis of variance) method to determine the average difference in blood glucose and total cholesterol levels and continued with Tukey's HSD post-hoc test to see real differences between treatment groups.

RESULTS

Simplisia powder weighing as much as 900 grams was extracted by the maceration method using 70% ethanol solvent for 3 days and stirred once every 24 hours. The extraction results were evaporated using a rotary evaporator at 600 °C and then thickened in a water bath to obtain a thick ethanol extract of sweet potato leaves of 245 g with a moisture content of 18.98%. The extract yield of 27.22% is in accordance with the Indonesian Herbal Pharmacopoeia, which states that the yield of a good extract is >10%. A phytochemical screening of sweet potato leaf extract was carried out to obtain information on the class of secondary metabolite compounds used as drugs that have pharmacological effects. The results of phytochemical screening are presented in **(**Table 1).

The negative control group experienced an increase in glucose and total cholesterol levels from day 7 to day 28, while the positive control group that received metformin alone and the sweet potato leaf extract test group, both single administration and combination with metformin, showed a decrease in blood glucose and total cholesterol levels up to day 28, as shown in (Figure 1-2). The higher the dose of SPLE, the greater the reduction in blood glucose and total cholesterol levels. The combination of ethanol extract of sweet potato leaves with metformin was significantly different from the single administration of ethanol extract of sweet potato leaves in reducing fasting

blood glucose levels but not significantly different in reducing total cholesterol.

Tabel 1: Phytochemical screening of purple sweet potato leaf ethanol extract.

Pemeriksaan	Reagent	Hasil
Alkaloid	Dragendroff	+
	Bouchardat	+
	Meyer	+
Flavonoid	Mg powder + Amil Alcohol + HCl	+
Glikosida	Molish + H2SO4	-
Saponin	Hot distilled water	+
Tanin	FeCl3	+
Steroid/Triterpenoid	Lieberman-Bouchar	+/-

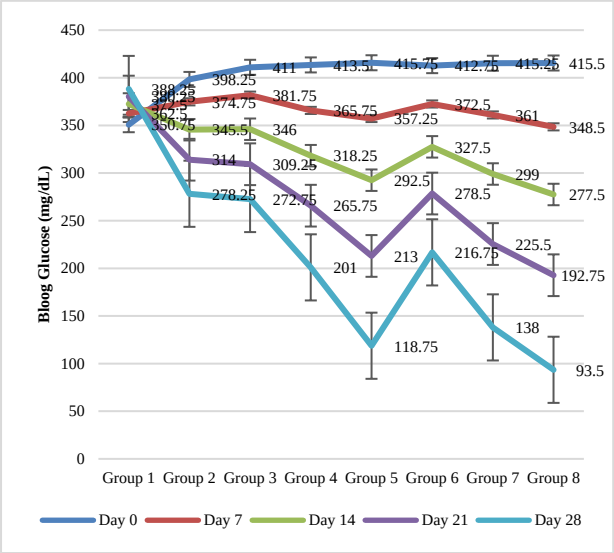

Figure 1: Blood glucose level from day 0 to day 28.

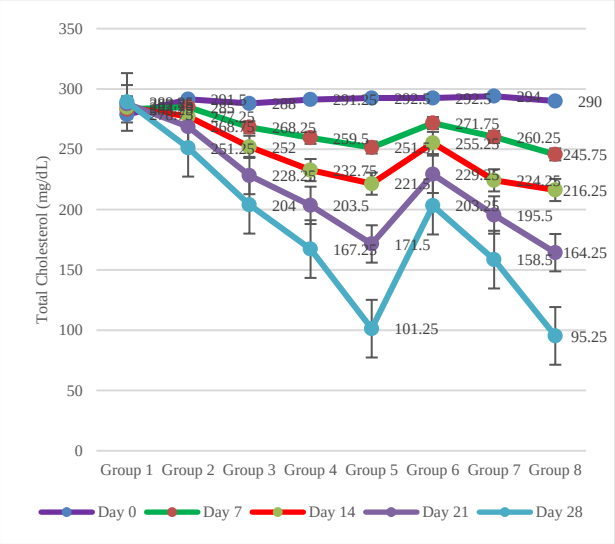

Figure 2: Total cholesterol from day 0 to day 28.

DISCUSSION

In this study, plasma glucose and total cholesterol increased ($p<0.05$) in high-fat diet and streptozotocin-induced diabetic rats. In the negative control group, KGD increased from day 7 to day 28. This was due to the induction of a high-fat diet and STZ.[13] STZ is a diabetogenic chemical compound that directly damages pancreatic beta cells.

Hypercholesterolaemia exacerbates the hyperglycaemic state. Elevated glucose levels cause ROS to accumulate in cells.[11] Sweet potato leaf aqueous extract 400 mg/kg BW is more effective than metformin in reducing blood glucose levels in streptozotocin-induced rats.[14] At a dose of 400 mg/kg BW, 70% ethanol extract showed maximal hypoglycaemic activity and non-toxicity in STZ-induced rats.[13]

Sweet potato leaves contain phenolic compounds, flavonoids, and anthocyanins, which are powerful antioxidants: free radical scavengers, metal chelators, and inhibitors of lipid peroxidation.[15] Sweet potato leaves contain phenolic acids, alkaloids, flavonoids, saponins, tannins, and anthocyanins, which have antioxidant activity against oxidative and free radical-mediated reactions.[13,15] Sweet potato leaf extract with 70% ethanol solvent contains the highest flavonoids and anthocyanins than 50% aceton solvent where 70% ethanol extract was used in this study. In the in vitro test, flavonoids from sweet potato leaf extract reduced blood glucose levels by inhibiting α-glucosidase, and flavonoids inhibited α-glucosidase 10.9 times more than acarbose.[13,16]

Anthocyanins are flavonoid phytopigments with antioxidant properties.[17] Previous research has shown that EDUJ is anti-hyperglycaemic by stimulating the secretion of glucagon-like peptide-1 (GLP-1), the antidiabetic mechanism of anthocyanins by stimulating GLP-1, increatin hormone, and triggering the proliferation of insulin hormone and pancreatic β-cells.[10,17] Saponins have hypoglycemic activity and prevent diabetic complications due to their antioxidant activity.[18] Ipomoea batatas leaf powder showed good antiradical activity and effectively reduced total cholesterol, triglyceride, and LDL cholesterol levels.[19-21]

Metformin is a glucose-lowering agent, and its primary mechanism is inhibition of hepatic gluconeogenesis through activation of adenosine monophosphate kinase (AMPK), which suppresses glucagon-stimulated glucose production and increases glucose uptake via glucose transporter type 4 (GLUT4) in muscle and liver cells.[22-24]

Limitations

This study is limited to measuring blood glucose and total cholesterol levels; therefore, it is necessary to study more lipid profiles, pancreatic histopathology, liver histopathology, and AMPK.

CONCLUSION

The combined effect of an ethanol extract of sweet potato leaves with metformin on blood glucose and total cholesterol in type 2 diabetes is better than that of a single administration of both metformin and an ethanol extract of purple sweet potato leaves in reducing blood glucose and total cholesterol levels.

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