

Phytochemical Analysis of Papaya, Mengkudu, Cassava, and Pearl Grass Leaf Extracts as Natural Anti-Hyperglycemic Agents

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Abstract: Hyperglycemia is a medical condition in which blood glucose levels exceed normal limits, and is a characteristic feature of diabetes mellitus (DM). This disease is characterized by high blood sugar levels due to impaired insulin production. This study aims to determine the effect of secondary metabolites contained in papaya leaf extract, noni leaf extract, cassava leaf extract, and pearl grass extract as antihyperglycemic agents. The research method used maceration with 70% ethanol solvent to obtain a thick extract, followed by phytochemical testing. This method also used a literature review to determine the effect of bioactive compounds in cassava leaf extract (*Manihot esculenta*), noni leaf extract (*Morinda citrifolia*), papaya leaf extract (*Carica papaya*), and pearl grass extract (*Hedyotis corymbosa*) as natural hyperglycemia agents. The results showed that the four extracts contained various secondary metabolites, namely flavonoids, alkaloids, tannins, phenolics, saponins, steroids, and triterpenoids. Papaya leaves had the best extract with complete secondary metabolites to overcome hyperglycemia. Although the three extracts, namely cassava, noni, and pearl grass, did not have complete secondary metabolite content like papaya, they contained flavonoids, phenolics, saponins, and alkaloids to treat hyperglycemia. Thus, these local plants have the potential to be developed as sources of raw materials for natural hyperglycemia phytopharmaceuticals

1 INTRODUCTION

Hyperglycaemia is a medical condition where an increase in blood sugar levels exceeds normal limits which can cause insulin resistance and disruption of pancreatic β -secretion to cause increased oxidative stress, this occurs because the formation of ROS exceeds its metabolic ability resulting in oxidative stress in the body and oxidative damage to tissues that cause chronic diseases to lead to basic complications including angiopathy in the vascular system and neuropathy in the nervous system. Hyperglycaemia is one of the hallmarks of

diabetes mellitus (Sari et al., 2018). Diabetes mellitus (DM) is a metabolic condition characterised by elevated blood glucose levels due to lack of insulin secretion, impaired insulin function, or a combination of both. A diagnosis of diabetes is made when fasting blood sugar levels exceed 126 mg/dL and blood sugar levels two hours after eating are more than 200 mg/dL. According to a report from the International Diabetes Federation (IDF), there are 371 million individuals aged between 20 to 79 years old suffering from DM worldwide. Indonesia ranks seventh with the highest prevalence of DM. The IDF also predicts that the number of DM cases will increase to 205

million among patients aged 40-59 years by 2035. Measurement of glycosylated haemoglobin (HbA1c) is used to monitor the average increase in blood glucose levels over the past 1-3 month period (Bakri et al., 2023).

Treatment of hyperglycaemia can be done through pharmacological therapy, which includes the administration of insulin and oral antidiabetic drugs, or through the use of traditional medicines that contain secondary metabolites with potential, such as flavonoids, alkaloids, saponins, terpenoids, tannins, steroids, polyphenols, and anthocyanins. These compounds play a role in inhibiting glucose transport in the gut, thereby lowering glucose levels. Various treatment approaches to control blood sugar levels and prevent complications in patients with diabetes mellitus include the use of hyperglycaemic drugs derived from plants (Santi et al., 2020). The use of medicinal plants as antioxidants has been widely researched. The selection of papaya leaves, cassava leaves, mengkudu leaves, and pearl leaves is based on literature showing that each has antioxidant and antidiabetic compounds. The variety of extracts is expected to have a synergistic effect in reducing oxidative stress and preventing spleen tissue necrosis due to hyperglycaemia. Phytochemical screening was conducted to determine the content of secondary metabolites in the plant (Gamse, 2002).

Noni leaf (*Morinda citrifolia*) is a leaf that can be used for medicinal purposes or can be consumed as a healthy drink. Noni leaves contain phytochemicals, such as phenolic acids, flavonoids, alkaloids, and polysaccharides. The content in noni can provide many benefits, one of which is the treatment of diabetes, hypertension and has antioxidant activity (Ramayani et al., 2021).

According to research (Rohman et al., 2006), antioxidant activity in noni leaves is influenced by the content of phenolic compounds and flavonoids. The phenolic content contained in noni leaf extract is 3.02% b/b GAE (Gallic Acid Equivalent) and the flavonoid content in noni leaf extract obtained through maceration method is 0.46% b/b QE (Quercetin Equivalent) (Ramayani et al., 2021). According to research (Wang et al., 2022) states that noni leaves can have potential as an anti-hyperglycemic natural medicine and the bioactive compounds contained in noni leaves are dominated by phenolics.

Papaya leaves (*Carica papaya*) contain compounds such as alkaloids, saponins, tannins, and flavonoids, so that papaya leaf extract can be used in herbal medicine (Rustiani et al., 2017). The statement supports research (Fakeye et al., 2007) that papaya leaves have antioxidant activity and can reduce blood sugar levels in rats at a dose of 5.0mg/200g. According to research (Zakaria et al., 2024) papaya leaves are able to reduce blood sugar levels or help control mild hyperglycaemia conditions. The antihyperglycaemic activity of these leaves is due to the content of chemical compounds such as flavonoids and saponins. Flavonoids work by reducing glucose absorption or increasing the body's tolerance to glucose. According to research (Irawan et al., 2020) Papaya leaf extract dissolved using ethanol has a phenolic content of 3.490 mgGAE/gram (Gallic Acid Equivalent) and flavonoid levels in papaya leaf extract, the total flavonoid content of papaya leaf ethanol extract was found to be 4.613 mgQE/gram (Quercetin Equivalent).

Cassava leaf extract (*Manihot esculenta*) has potential as an antihyperglycaemia because of its

flavonoid content that can help reduce blood glucose levels. Flavonoids work by several mechanisms such as increasing insulin secretion from pancreatic beta cells, increasing glucose uptake by peripheral tissues, regulating enzyme activity associated with carbohydrate metabolism and acting like insulin that can affect insulin signalling pathways. Thus, the flavonoid content in cassava leaves can help control blood sugar levels and become an alternative antihyperglycaemia treatment (Warditiani et al., 2015). According to research (Okoro, 2020), cassava leaf extract dissolved using ethanol has a phenolic content of 0.82 mgGAE/gram (Gallic Acid Equivalent) and flavonoid levels in cassava extract obtained 0.64 mgQE/gram (Quercetin Equivalent).

Pearl grass extract (*Hedyotis corymbosa*) is an herbal drink that has often been used since ancient times, this pearl grass leaf has many benefits, one of which is as an antidiabetic due to the saponin content in the pearl grass leaf, besides saponins, some of the contents contained in pearl leaves include hentriacontane, stigmasterol, ursolic acid, oleanolic acid, ß-sitosterol, sitosterol-D- glucoside, p-coumaric acid, flavonoids (Soemardji et al., 2015). Extracts from pearl grass contain flavonoids and saponins. Based on research conducted by (Mangallo et al., 2019), flavonoid compounds and saponins show the ability to inhibit the α - glucosidase enzyme, increase insulin response, and control blood glucose levels because they have antidiabetic effects. Flavonoids found in pearl grass leaves have antioxidant abilities that contribute to lowering blood sugar levels by increasing sensitivity to insulin, besides that, saponins and tannins have a function as regulators of the immune system by increasing the proliferation and activity of immune cells. According to research

(Wahyuni et al., 2018) Pearl grass leaf extract dissolved using ethanol has a phenolic content of 154 mgGAE/gram (Gallic Acid Equivalent) and flavonoid levels in pearl grass extract obtained 1.78 mgQE/gram (Quercetin Equivalent).

Based on previous research, it can be concluded that extracts from papaya leaves, cassava leaves, mengkudu leaves, and pearl grass have the ability as antidiabetic and antihyperglycemic agents. Each plant has a unique way of lowering blood sugar, regulating body weight, and affecting the immune system, which includes the number and variety of leucocytes. Although each plant showed good results, more studies are needed to elucidate the molecular mechanism and the best dose for the use of some extracts as antidiabetic agents. Therefore, this study aims to determine the effect of secondary metabolite content and antioxidant activity contained in papaya leaf extract, mengkudu leaf, cassava leaf, and pearl grass as antihyperglycemic agents.

2 METHOD

Location and Time of Research

This research was conducted at the Laboratory of Basic Chemistry and Basic Biology Campus II Sunan Ampel State Islamic University Surabaya from June to July 2025.

Tools and Materials

Tools and materials used in this study include beakers, volumetric flasks, aluminium foil, paper, analytical scales, Erlenmeyer, stirring rods, test tubes, spatulas, measuring cups, filter paper and glass funnels. The materials used in this study such as various materials of papaya leaves, pearl leaves, noni

leaves, cassava leaves, distilled water and 70% ethanol.

Extraction

Extraction was carried out using the maceration method. The maceration method was carried out by soaking the leaf sample powder using distilled water solvent for 2x24 hours with occasional stirring. Weighed 250 grams of powder, measured 70% ethanol solvent as much as 1250 ml with a measuring cup, then poured the sample into a glass bottle, stirred briefly and closed the glass bottle tightly so as not to evaporate. The mixture was sonicated with a sonicator for 30 minutes. The mixture was allowed to stand for 2x24 hours with occasional stirring. After 2x24 hours, the result was filtered with filter paper. The filtrate is evaporated using a rotary evaporator with a temperature of about 50°C - 55°C and rotated at a speed of 60 - 70 rpm to remove the solvent so that the extract of natural ingredients is obtained (Agustina, 2017).

Phytochemical Test

- Alkaloid Test

The ethanol extract of each leaf was weighed as much as 0.5gram which was put into a test tube and added 1% HCl as much as 0.5 mL, then added 1-2 drops of dragendorff. If it produces an orange colour, it shows positive alkaloid (Agustina et al., 2018).

- Flavonoid Test

The ethanol extract of each leaf is weighed as much as 200 mg or 0.2 grams and put into a test tube. Added 5 mL of ethanol and heated for 5 minutes. Added a few drops of concentrated HCl and added 0.2gram of magnesium. If a dark red (magenta)

colour appears, it shows positive flavonoids (Agustina et al., 2018).

- Saponin Test

The saponin test is carried out by weighing 0.5 grams of leaf extract and the sample is put into a test tube. The leaf extract was added to hot water and cooled. The cooled mixture is shaken for 10 minutes until foam is formed, then 2 N HCl is added. If foam is formed and 2 N HCl is added, the foam remains, indicating positive saponin (Agustina et al., 2018).

- Phenolic Test

Leaf extract was weighed as much as 0.5gram and put into erlenmeyer, then added 70% ethanol as much as 10 mL. Taken 1 mL of the solution formed and put into a test tube. After that, 2 drops of 5% FeCl₃ solution were added. Phenolic positivity is indicated by the formation of green or bluish green colour (Agustina et al., 2018).

- Tannin Test

Leaf extract was weighed as much as 0.5gram which was put into a test tube and added distilled water as much as 3 mL. Cassava leaf extract then added FeCl₃ 1% as much as 2 drops. Positive results of tannin are indicated when it forms a bluish green colour (Agustina et al., 2018).

- Steroid and Triterpenoid Test

The leaf extract was weighed as much as 0.5gram and put into a test tube, then added CHCl₃ as much as 0.5 mL and acetic acid as much as 0.5 mL. Concentrated H₂SO₄ was added as much as 2 mL through the test tube wall.

The extract is declared positive for triterpenoids if a purple-red colour is formed (Novia, 2020). While positive for steroids if it produces green or blue colour (Mondong, 2015).

The Relationship Between Chemical Compounds and Blood Sugar Levels: Literature Review

This method of measuring blood sugar levels uses a literature review. The process of referencing and researching journals uses secondary data obtained from the results of research conducted by previous researchers. The secondary data sources referred to are articles or journals.

3 RESULT

Table 1. Phytochemical Screening Results of Papaya, Noni, Cassava, and Pearl Leaf Extracts. (Source: Personal Data, 2025)

Compound	Results for each extract			
	Papaya	Noni	Cassava	Pearl Grass
Alkaloid	+	+	+	+
Flavonoid	+	+	+	+
Fenolik	+	+	+	+
Tanin	+	+	+	-
Saponin	+	+	-	-
Steroid	+	-	-	-
Triterpenoid	+	+	+	+

Table 2. Literature Review on the Effects of Papaya Leaf, Noni, Cassava, and Pearl Grass Extracts on Hyperglycemia

Title	Author	Method	Results
Papaya Leaves (<i>Carica papaya</i>)			
Testing the Effect of Papaya Leaf Extract on Streptozotocin-Induced Blood Glucose Reduction in White Mice	(Wulandari et al., 2022).	This study used in vivo experiments on 20 male white rats induced by alloxan and given papaya leaf ethanol extract (<i>Carica papaya</i> L.) with varying doses of 100, 200, and 300 mg/kgBW, then their blood glucose levels were measured.	Papaya leaf ethanol extract at a dose of 300 mg/kg BW can provide the most effective reduction in blood glucose levels, approaching the effect of the control drug glibenclamide.
Antihyperglycemic and hypolipidemic activities of aqueous extract of <i>Carica papaya</i> Linn. leaves in alloxan-induced diabetic rats	(Yasmeen & Prabhu 2012).	The experimental research method was carried out by administering water extract of <i>Carica papaya</i> Linn. leaves to albino rats induced with diabetes with alloxan monohydrate (120 mg/kg, ip) for 21 days, with measurements of blood sugar levels and lipid profiles to assess the antihyperglycemic and hypolipidemic activities of the extract.	Papaya leaf extract has a potential antihyperglycemic effect on diabetic rats because papaya leaf extract has a dose of 400 mg/kg which can significantly reduce blood sugar levels from the first day to the 21st day, can reduce blood levels and triglycerides in diabetic rats.

Anti-Diabetic Efficacy and Phytochemical Screening of Methanolic Leaf Extract of Pawpaw (<i>Carica papaya</i>) Grown in North Central Nigeria	(Ogundele et al., 2017)	In vitro experimental research method with methanol extraction of <i>Carica papaya</i> leaves and testing of anti-diabetic activity in vitro through inhibition of α -amylase enzyme, glucose uptake by yeast cells, and inhibition of non-enzymatic hemoglobin glycosylation.	Papaya leaf methanol extract contains bioactive compounds such as tannins, saponins, terpenoids and alkaloids, and shows significant anti-diabetic activity in vitro with increased glucose uptake, inhibition of α -amylase up to 25.2%, and inhibition of hemoglobin glycosylation, proving the therapeutic potential of this extract for the development of diabetes drugs.
Comparison of Papaya Leaf Extract (<i>Carica Papaya</i> L) and Metformin Administration on Reducing Blood Glucose Levels in Mice (<i>Mus Musculus</i>) Induced by Alloxan.	(Damayanti et al., 2022).	This study uses a literature review with a narrative review design to compare the effects of papaya leaf extract (<i>Carica papaya</i>) and metformin on reducing blood glucose levels in alloxan-induced mice.	The results showed that papaya leaf extract had antihyperglycemic activity at doses of 150–600 mg/kg BW, but its effectiveness was still lower than metformin.
Assessments of phytochemicals and hypoglycemic activity of leaves extracts of <i>Carica papaya</i> in diabetic mice.	Sobia et al., 2016	The method used was papaya leaf extraction with various solvents followed by hypoglycemic testing on diabetic rats and streptozotocin induction as well as phytochemical analysis.	The results obtained showed that papaya leaf ethanol extract had significant hypoglycemic activity, improved lipid profiles, liver enzymes, and blood cell levels in diabetic rats, and contained high levels of flavonoid quercetin as the main bioactive component.
Cassava Leaves (<i>Manihot esculenta</i>)			
Two Extracts From (<i>Manihot Esculenta</i>) Leaves Efficiently Inhibit α -Glucosidase and α -Amylase: A New Approach for the Management of Diabetes	(Okoro, 2020)	The method used in vitro was due to the evaluation of the inhibitory activity of α -glucosidase and α -amylase using ethanol and acetone extracts from cassava leaves, as well as measuring the total phenolic and flavonoid content.	The results showed that the ethanol extract of cassava leaves (<i>Manihot esculenta</i>) had stronger α -glucosidase and α -amylase inhibitory activity than the acetone extract, with an α -glucosidase IC ₅₀ value of 0.77 mg/mL which was better than Acarbose; the phenolic and flavonoid content was also higher in the ethanol extract, so this extract has the potential as an antihyperglycemic and antioxidant agent for diabetes
Antidiabetic (α -amylase and α glucosidase) and anti-obesity (lipase) inhibitory activities of edible cassava (<i>Manihot esculenta</i> Crantz) as measured by in vitro gastrointestinal digestion: effects of phenolics and harvested time	(Laya et al., 2022)	The method used was in vitro testing with the inhibitory activity of the enzymes α -amylase, α -glucosidase, and lipase from cassava leaf extract (<i>Manihot esculenta</i>) processed by simulating gastrointestinal digestion, as well as analysis of phenolic and flavonoid content.	The brief results in this journal show that cassava leaves (<i>Manihot esculenta</i>) contain bioactive compounds, such as flavonoids, stilbenes, tannins, and saponins, which have significant inhibitory activity against α -amylase and α -glucosidase enzymes, both in free, bound, and bioaccessible fractions after in vitro digestion. This activity has the potential to lower blood glucose levels by inhibiting carbohydrate digestive enzymes, thus functioning as an antidiabetic and antihyperglycemic agent.
Cassava (<i>Manihot esculenta</i>): A Systematic Review for the Pharmacological Activities, Traditional Uses, Nutritional Values, and Phytochemistry	(Mohidin et al., 2023)	Systematic review by analyzing various studies related to the pharmacological activity of cassava plants (<i>Manihot esculenta</i> Crantz).	The research results show that cassava has various pharmacological potentials, including anticancer, anti-inflammatory, antidiabetic, hepatoprotective, immunomodulatory, and antioxidant activities.
Determination of Toxicity and Hypoglycemic Effect in Alloxan induced Diabetic Mice of <i>Manihot esculenta</i> Crantz (Fam. Euphorbiaceae) Aqueous Crude Leaf Extract and its Fractions	(Bautista et al., 2025)	Oral administration of plant extracts to mice induced with diabetes, then measuring blood glucose levels and other biochemical parameters to evaluate the hypoglycemic effect	Oral administration <i>Manihot esculenta</i> (cassava) leaf water extract to streptozotocin-induced diabetic mice significantly reduced blood glucose levels.

Phytochemical Content and Antidiabetic Properties of Most Commonly Used Antidiabetic Medicinal Plants of Kenya	(Muema et al., 2023)	The research method is a literature review of the phytochemical profile and antidiabetic activity of medicinal plants, including in vitro and in vivo studies of extracts and isolated compounds of cassava leaves.	Ethanol and acetate extracts of cassava leaves showed inhibitory activity against α -glucosidase and α -amylase enzymes in a dose-dependent manner, with antihyperglycemic potential through various
Bioguided Optimization of the Nutrition-Health, Antioxidant, and Immunomodulatory Properties of <i>Manihot esculenta</i> (Cassava) Flour Enriched with cassava Leaves	(Boukheret et al., 2023)	Bioguided comparative study with regular cassava flour formulation and cassava flour enriched with 30% cassava leaf powder, testing the nutritional content, in vivo glycemic index, and potential antioxidant and immunomodulatory activities using macrophage cultures.	The result obtained showed that the addition of cassava leaves reduced the glycemic index of flour by up to 20% and increased the fiber, phenolic, carotenoid content as well as antioxidant and anti-inflammatory activities significantly, so that flour with cassava leaves is recommended for the management of blood glucose profiles and inflammation related to diabetes.
Pearl Leaf (<i>Hedyotis corymbosa</i>)			
Screening of Secondary Metabolite Compounds of Pearl Grass Extract (<i>Hedyotis Corymbosa</i> (L.) Lamk.) Using GC-MS Method	(Wijayanti, 2017)	Pearl grass (<i>Hedyotis corymbosa</i>) was extracted using hexane solvent, then analyzed using Gas Chromatography–Mass Spectrometry (GC-MS) to identify its secondary metabolite compounds.	GC-MS analysis successfully identified 20 secondary metabolite compounds, including catechol, camphene, limonene, myrcene, pinene, camphor, cineole, geraniol, citronellol, gallic acid, ascorbic acid, β -caryophyllene, β -elemene, β farnesene, α -selinene, apigenin, kaempferol, luteolin, catechin, and betulinic acid. The three compounds with the highest composition were gallic acid (18.583%), catechin (16.616%), and geraniol (12.876%). These compounds have various important biological functions, such as antidiabetic, antioxidant, antibacterial, antiinflammatory, anticancer, antitumor, antileukemic, hepatoprotective, and immunomodulatory.
Hypoglycemic and hypolipidemic effects of <i>Oldenlandia corymbosa</i> against alloxan induced diabetes mellitus in rats	(ELWON et al., 2020)	The plant water extract was administered to alloxan-induced diabetic rats and blood glucose levels and antioxidant parameters were measured for 14 days.	The results of the study showed that pearl grass extract significantly reduced blood glucose levels, increased antioxidant enzymes, improved lipid profiles, and showed improvements in pancreatic structure in diabetic rats.
Evaluation of in vitro enzyme inhibitory, anti-inflammatory, antioxidant, and antibacterial activities of <i>Oldenlandia corymbosa</i> L. and <i>Oldenlandia umbellata</i> L. whole plant extracts	(Divya et al., 2023)	The administration of ethanol and water extracts was tested in vitro for the ability to inhibit the enzymes α -amylase and α -glucosidase as an antihyperglycemic mechanism.	Administration of pearl grass extract using ethanol solvent resulted in significant inhibition of α -amylase and α -glucosidase with IC ₅₀ close to standard acarbose, and showed antihyperglycemic potential.
Botanical features, phytochemical and pharmacological overviews of <i>Oldenlandia corymbosa</i> Linn.: A brief review	(Das et al., 2019).	In vitro tests using ethanol extracts from the aerial parts of the <i>Oldenlandia corymbosa</i> plant and antidiabetic activity tests through inhibition of the α -glucosidase enzyme, which plays a role in the breakdown of carbohydrates into glucose.	Ethanol extract of pearl grass showed α glucosidase inhibitory activity of up to 90%. This indicates strong potential as an antidiabetic agent because it inhibits glucose absorption in the intestine and prevents blood sugar spikes so that pearl grass has the potential to be developed as an antihyperglycemic agent.
Noni leaves (<i>Morinda citrifolia</i>)			

Anti Diabetic Effect of Fruit Juice of <i>Morinda Citrifolia</i> (Tahitian Noni Juice) on Experimentally Induced Diabetic Rats	(Horsfal et al., 2008)	Administration of noni to Sprague-Dawley rats whose diabetes was induced with alloxan, with periodic blood sugar level measurements to evaluate the antihyperglycemic effect.	Preventive administration of noni juice before and after diabetes induction in rats can reduce elevated blood glucose levels caused by Alloxan induced damage to pancreatic beta cells. Noni juice has potential antihyperglycemic effects, possibly related to its antioxidant activity and protection of pancreatic beta cells from oxidative damage. However, discontinuation administration hyperglycemia. resulted of in a the return juice of
One Plant, Many Uses: A Review of the Pharmacological Applications of <i>Morinda citrifolia</i>	(Torres et al., 2017)	In vivo experiments with the administration of ethanol extract of noni leaves (<i>Morinda citrifolia</i>) to streptozotocin-induced diabetic rats, then analyzed for biochemical parameters, histopathology, and antioxidant activity.	The results of the study showed that noni leaf extract (<i>Morinda citrifolia</i>) was able to reduce blood glucose levels, repair histological damage to the pancreas, and increase antioxidant capacity, thus having the potential to be a natural antidiabetic agent.
Biochemical evaluation of antihyperglycemic and antioxidative effects of <i>Morinda citrifolia</i> fruit extract studied in streptozotocin induced diabetic rats	(Mahadeva Subramanian, 2009)	&The method used in this journal is by administering ethanol extract of <i>Morinda citrifolia</i> fruit (300 mg/kg BW/day orally) to male Wistar rats induced with diabetes with streptozotocin for 30 days, then biochemical parameters were analyzed (blood glucose, hemoglobin, HbA1c, plasma insulin, urea, creatinine, liver enzymes, and enzymatic and non-enzymatic antioxidant status).	The results of the study showed that noni fruit extract significantly reduced blood glucose levels, HbA1c, urea, creatinine, and improved insulin levels, hemoglobin, total protein, liver enzyme activity, and increased antioxidant status, thus having antihyperglycemic, antioxidant, and hepatoprotective effects on diabetic rats.
Cassava (<i>Manihot esculenta</i>): A Systematic Review Pharmacological for the Activities, Traditional Uses, Nutritional Values, and Phytochemistry	(Mohidin et al., 2023)	Systematic review by analyzing various studies related to the pharmacological activity of cassava plants (<i>Manihot esculenta</i> Crantz).	The research results show that cassava has various pharmacological potentials, including anticancer, anti-inflammatory, hepatoprotective, antidiabetic, immunomodulatory, antioxidant activities.
Determination of Toxicity and Hypoglycemic Effect in Alloxan induced Diabetic Mice of <i>Manihot esculenta</i> Crantz (Fam. Euphorbiaceae) Aqueous Crude Leaf Extract and its Fractions	(Bautista et al., 2025)	Oral administration of plant extracts to mice induced with diabetes, then measuring blood glucose levels and other biochemical parameters to evaluate the hypoglycemic effect	Oral administration of <i>Manihot esculenta</i> (cassava) leaf water extract to streptozotocin nicotinamide-induced diabetic mice significantly reduced blood glucose levels.

Papaya leaf extract (*Carica papaya*.) is widely used by some people as a natural medicine because it is known to have many benefits for body health. Table

1. Explaining that papaya leaf extract positively contains alkaloids, flavonoids, phenolics, tannins, saponins, steroids and triterpenoids. This is confirmed by research According to research (Airaodion et al., 2019) papaya leaves are known to contain various bioactive compounds that can increase total antioxidant capacity in the blood and

reduce lipid peroxidation levels. The antihyperglycemic effect of papaya leaf extract is thought to originate from the content of bioactive compounds such as flavonoids, alkaloids, and other phenolic compounds that have antioxidant activity and can inhibit carbohydrate hydrolyzing enzymes (α -amylase and α -glucosidase) in the digestive tract, thereby slowing glucose absorption and reducing post-meal blood sugar disorders. According to research (Nyakundi & Yang, 2023) in addition to playing a role in lowering glucose levels. This extract

is able to stimulate increased insulin production in pancreatic cells while protecting beta cells from damage triggered by diabetes. In test animals, especially diabetic rats, papaya leaves have been shown to significantly reduce blood sugar levels.

Noni leaf extract (*Morinda citrifolia*) contains various bioactive compounds such as flavonoids (quercetin, kaempferol) which have antioxidant, anti-inflammatory, analgesic, and antidiabetic properties (Shashikumar et al., 2022). According to research (de Oliveira Fernandes et al., 2023) Noni extract (*Morinda citrifolia* L.) shows antihyperglycemic or antidiabetic effects as shown by a significant decrease in blood glucose levels in streptozotocin (STZ)-induced diabetic rats after chronic supplementation for 60 days, reducing blood triglyceride levels of diabetic rats to near normal conditions. In addition, it improves insulin resistance as measured by the TyG index (triglyceride-glucose index). According to research (Muema et al., 2023). Cassava extract (*Manihot Esculenta*) in phytochemical studies shows that cassava leaf extract contains bioactive compounds such as flavonoids and phenolics that play a role in antidiabetic activity. Ethanol and acetone extracts of cassava leaves have been shown to exhibit antihyperglycemic activity by significantly inhibiting α -glucosidase and α -amylase enzymes in in vitro tests, which contribute to controlling blood glucose levels by slowing down carbohydrate digestion.

According to research (Atmarani, RE, & Sulistyani, 2025), pearl grass extract (*Hedyotis corymbosa* L.) has high flavonoid content and antioxidant activity, which can contribute to antihyperglycemic or antidiabetic effects. Through the fermentation process with lactic acid bacteria, the

total flavonoid content and antioxidant activity of the polyherbal extract containing pearl grass increased significantly, which is believed to help reduce blood glucose levels and improve metabolic health.

4 CONCLUSIONS

Based on the results of phytochemical screening and literature review, ethanol extracts of papaya leaves (*Carica papaya*), noni leaves (*Morinda citrifolia*), cassava leaves (*Manihot esculenta*), and pearl grass (*Hedyotis corymbosa*) have been shown to contain various bioactive compounds, such as flavonoids, alkaloids, phenolics, tannins, saponins, steroids, and triterpenoids. These compounds have antioxidant and antidiabetic activities that play a role in lowering blood glucose levels through the mechanism of inhibiting carbohydrate digestive enzymes, increasing insulin secretion, and protecting pancreatic β cells from damage due to oxidative stress. Thus, these four local leaf extracts have great potential to be developed as natural antihyperglycemic agents that support the management of diabetes mellitus while preventing complications through antioxidant activity. However, further research, especially in vivo and clinical trials, is still needed to determine the optimal dosage, safety, and effectiveness in long-term use.

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