LenteraBio
Berkala Ilmiah Biologi

LenteraBio, 2026; Volume 15, Issue 2: 175-182

p-ISSN: 2252-3979 e-ISSN: 2685-7871
https://journal.unesa.ac.id/index.php/lenterabio/index

Antidiabetic Effect of *Abelmoschus esculentus* L. on Alloxan-Induced Type 1 Diabetic Mice

Gusti Ayu Mirah Dwidaputri [1], Iriani Setyawati [2]*, Sang Ketut Sudirga [3]
[1]Biology Master Program Alumni, Faculty of Mathematics and Natural Sciences, Universitas Udayana, Bukit Jimbaran, Badung, Bali
[2]Biology Study Program, Faculty of Mathematics, Natural and Earth Sciences, Universitas Negeri Manado, Tondano, North Sulawesi
[3]Biology Study Program, Faculty of Mathematics and Natural Sciences, Universitas Udayana, Bukit Jimbaran, Badung, Bali
*Corresponding author, e-mail: irianisetyawati@unima.ac.id

Article History:
Received:
30-July-2025
Revised:
29-May-2026
Available online:
31-May-2026
Published regularly:
31-May-2026

Abstract
Diabetes mellitus type 1 is a metabolic condition characterized by inadequate regulation of glucose, fats, and proteins as a result of insufficient insulin levels. Insulin helps tissue in glucose uptake for energy and fat synthesis. This study investigated the chemical compounds in the 96% ethanol extract of (*Abelmoschus esculentus* pods, evaluated its effects on fasting blood glucose levels, and examined its impact on the pancreatic histology of male diabetic mice (*Mus musculus* L.) induced with alloxan. Twenty five mice were divided into five groups: K(-) (negative control with distilled water), K(+) (positive control with metformin), *A. esculentus* extract treatments, namely 200, 300, and 400 mg/kg bw (P1, P2, P3 respectively). Results showed that *A. esculentus* extract contains flavonoid and alkaloid, the predominant active compound identified was 2(1H)-Pyridinone, Hydrazone, Dihydrochloride (CAS). The extract has potential as an antidiabetic agent in hyperglycemic-induced mice, demonstrated by its ability to lower blood glucose levels, increase body weight, and improve the pancreatic histological structure of the Langerhans islet. The dose of 300 mg/kg bw showed the best effectiveness in improving the histological structure of the pancreas, while dose of 400 mg/kg bw provided a reduction in blood glucose levels that was closest to normal.

Keywords: Antidiabetic agent; good health and well-being; green okra
How to Cite: Dwidaputri GAM, Setyawati I, Sudirga SK, 2026. Antidiabetic Effect of Abelmoschus esculentus L. On Alloxan-Induced Type 1 Diabetic Mice. *LenteraBio;* 15(2): 175-182
DOI: https://doi.org/10.26740/lenterabio.v15n2.175-182

INTRODUCTION

Diabetes mellitus (DM), commonly known as diabetes, results from insufficient insulin secretion, impaired insulin function, or a combination of both. Importantly, insulin serves a crucial role as an anabolic hormone, affecting the metabolism of carbohydrates, lipids, and proteins (Poznyak et al., 2020). According to Utami (2018), the phytochemical groups in plant are able to serve as antioxidants to counteract free radicals reduce the risk of degenerative diseases such as diabetes mellitus.

Type 1 Diabetes Mellitus (T1DM) is a autoimnmune condition where the immune system mistakenly attacks and destroys the insulin-producing β-cells in the pancreas. It is well recognized that individuals with Type 1 Diabetes Mellitus (T1DM) experience progressive dysfunction of pancreatic β-cells, leading to an inadequate capacity to produce and secrete insulin. Furthermore, pancreatic α-cell dysfunction has emerged as a key feature of T1DM pathophysiology, resulting in inappropriate glucagon secretion. This dysregulation further disrupts glucose homeostasis, thereby aggravating hyperglycemia and contributing to the metabolic disturbances associated with the disease (Hughes and Narendran, 2014; Sims et al., 2020). This results in insulin deficiency, meaning those affected will need to rely on insulin therapy for the rest of their lives. The number of people diagnosed with T1DM is on the rise globally, and cases are increasing across various populations. This growing trend has sparked greater interest in finding treatments that target the autoimmune aspects of T1DM besides controlling high blood sugar levels (Bell and Lain, 2025).

Recent advances in diabetes research increasingly emphasize the role of oxidative stress and inflammation in the development of diabetes mellitus, particularly in β-cell dysfunction and damage. In this context, natural products rich in bioactive compounds have received significant attention as

OPEN ACCESS CC BY NC

potential complementary therapies. Among these products, *Abelmoschus esculentus* L. or okra, has been identified as a promising plant. *A. esculentus* is a fiber-rich plant believed to contain antioxidant and anti-diabetic properties. *A. esculentus* contains phenolic and flavonoid compounds, specifically quercetin-3-O-ß-D-glucopyranosyl-(1→6)-ß-D-glucopyranoside and quercetin 3-O-ß-D-4''-O-methyl-ß-D-glucopyranoside (Astati and Kasmawati, 2017). *A. esculentus* pods are high in flavonoids that act as antioxidants (Irshad et al., 2018; Anjani et al., 2018), while antioxidant treatment reduces oxidative stress (Sherif and Al-Gayyar, 2013). Green *A. esculentus* pods contain polysaccharides that help modulate the immune response against bacteria, *Staphylococcus aureus* infections (Wahyuningsih et al., 2017).

Despite these promising developments, the integrated effects of 96% ethanol extract of *A. esculentus*, on both metabolic outcomes (blood glucose levels) and histological structural changes in pancreatic tissue of male mice (*Mus musculus* L.) induced with alloxan has not been examined. Therefore, investigating its dual role in regulating blood glucose levels and maintaining pancreatic histology represents a crucial advance in the development of plant-based therapeutic strategies for diabetes management.

MATERIALS AND METHODS

This study used fresh green *A. esculentus,* measured approximately 10-15 cm, acquired from vendors at Badung Market Denpasar, Bali. *A. esculentus* pods were thoroughly washed with running water, air-dried without direct sunlight, and then cut into small pieces. Subsequently, the dried pieces of *A. esculentus* were blended into a powder. A total of 800 g of *A. esculentus* powder was macerated for 72 hours using 96% ethanol as solvent. After 72 hours, the extract was filtered to separate the residue from the filtrate. The maceration process was repeated five times on the residue of the *A. esculentus* extract until the residue was colorless. The obtained filtrate was then evaporated using a vacuum rotary evaporator at 40°C, resulting in a thick ethanol extract (crude extract) (Wardani et al., 2017).

Preliminary qualitative phytochemical screening was conducted on the plant extracts to detect major secondary metabolites. Alkaloids were identified by dissolving extracts in dilute acid and observing precipitate formation with Mayer's or Wagner's reagent (precipitation indicated alkaloid). Steroids were screened using the Liebermann–Burchard or Salkowski test, in which green to bluish-green layer with chloroform-acetic anhydride and sulfuric acid indicates steroids. Phenolic compounds and tannins were detected by adding 1% ferric chloride solution, with blue-black/greenish coloration indicated positive results. Saponins were tested by vigorously shaking the extract with distilled water and observing stable froth formation. Flavonoids were identified using the Shinoda (magnesium–hydrochloric acid) test. In this method, flavonoid compounds are reduced by magnesium powder in an acidic medium containing concentrated hydrochloric acid (HCl), producing a red, orange, or pink color as a positive indication of the presence of flavonoids. All assays used standard qualitative reagents and observations of color changes/precipitates to confirm presence of each metabolite class (Nortjie et al., 2022). Further identification of active compounds in the 96% ethanol extract of green *A. esculentus* was conducted using Gas Chromatography Mass Spectrometry (GC-MS QP2010 Ultra). This identification involved comparing the mass spectra of each peak with those of known compounds in the GC-MS database/library (NIST).

The antioxidant activity of the 96% ethanol extract of green *A. esculentus* was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) method. A 50 µM DPPH solution was prepared, and methanol was used as the solvent and blank. The absorbance of the reaction mixture was measured at 517 nm using a spectrophotometer. Antioxidant activity was expressed as the IC_{50} value, defined as the concentration of extract required to inhibit 50% of DPPH radical activity, calculated from the percentage of inhibition at various concentrations (Molyneux, 2004). The category of IC_{50} values as antioxidants are very strong (< 50 ppm), strong (50-100 ppm), moderate (101-150 ppm), weak (151-200 ppm), or inactive (>500 ppm) (Utami, 2018).

This research was an experimental study employing a post-test controlled group design. It utilized a Completely Randomized Design that included a negative control, a positive control, and three extract dose treatments, each with eight replications. The test subjects used in this study were male mice (*Mus musculus* L.) aged 2-3 months, with an average body weight of ± 25 g. The mice were acclimated for 1 week on standard mouse feed and ad libitum access to drinking water (refilled daily). The mice were housed in a well-ventilated room, in cages measuring 40x30x20 cm, with the cage floor lined with rice husks and sawdust, which were replaced twice a week. Each cage contained 2-3 mice, with room temperatures ranging from 28 to 32°C. Cage cleaning was performed twice a week to maintain the health of the experimental animals. Lighting was regulated with a 12-hour light and 12-hour dark cycle

(the light cycle commenced at 06:00 AM and continued until 06:00 PM). Following the acclimatization process, treatment was administered.

Induction of alloxan at a dose of 130 mg/kg body weight was performed on all mice via injection on the eighth day. During the treatment period (28 days), the negative control (K-) received standard feed and a placebo (2 mL of distilled water) in the morning. The positive control (K+) was given standard feed and metformin dissolved in distilled water via a feeding tube in the morning. Treatments P1, P2, and P3, in addition to standard feed, were also administered 96% ethanol extract of *A. esculentus* at doses of 200 mg/kg body weight (P1), 300 mg/kg body weight (P2), and 400 mg/kg body weight (P3), all of which were dissolved in distilled water and given in the morning. The administration of green *A. esculentus* extract was conducted using the gavage method, which involved oral administration via a feeding tube at a volume of 0.2 mL per animal per day.

The measurement of fasting blood glucose levels was conducted on the tenth day, following the induction of hyperglycemic in mice via alloxan. This is subsequently followed by weekly fasting blood glucose measurements for four weeks. The fasting blood glucose was measured after a 12 to 16-hour fast, with blood samples taken from the tail and analyzed for glucose levels using a glucometer (GlucoDr Korea).

Histological examination of the pancreatic tissue in mice was performed to assess the antidiabetic effects of green *A. esculentus* extract. Histological preparation of the pancreas included tissue processing, Hematoxylin-Eosin (HE) staining, and result interpretation. Histopathological observation and evaluation were carried out using a light microscope. Observations were made on 10 fields of view for each pancreatic organ. The diameter of the islets of Langerhans was measured from five randomly observed islets (Ermayanti et al., 2023; Setyawati, 2019).

Data analysis was conducted using statistic test in SPSS version 22. Initially, the body weight data were assessed for normality using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Statistical analysis used One-Way Analysis of Variance (ANOVA) followed by Duncan's Multiple Range Test (DMRT). Figure 1 presents the complete procedure of this study.

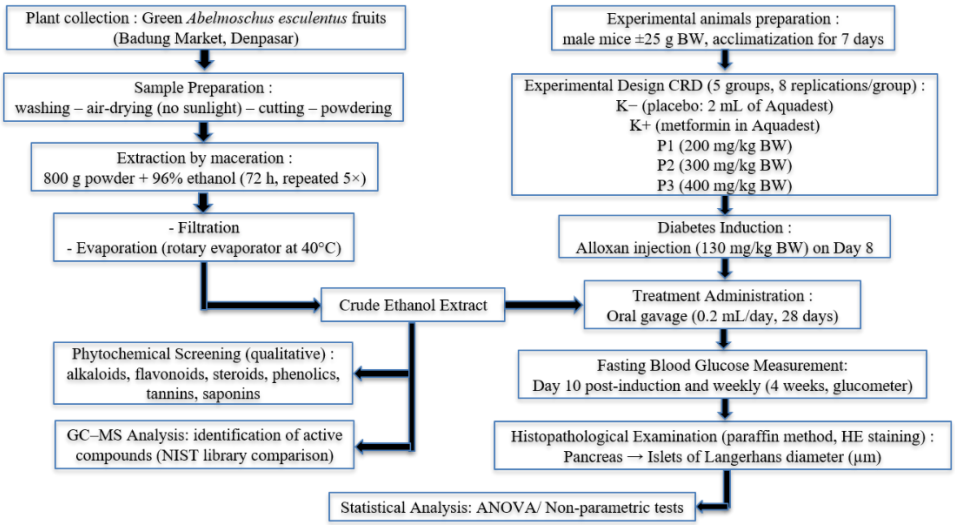

Figure 1. Research procedure

RESULTS

The results of the phytochemical analysis indicate that the 96% ethanol extract of green *A. esculentus* qualitatively tests positive for the presence of alkaloids, steroids, phenolics, saponins, flavonoids, and tannins. Meanwhile, the extract did not contain terpenoid compounds (Table 1).

Table 1. Content analysis of the 96% ethanol extract of green *A. esculentus*

No	Secondary Metabolite	Indicators	Content
1	Alkaloid	White deposit	+
2	Steroid	Dark green color	+++
3	Phenolic	Greenish color	+++
4	Saponin	Foam	++
5	Flavonoid	Red color	++
6	Tannin	Light blue color	+

Further identification of active compounds in the 96% ethanol extract of green *A. esculentus* was carried out using Gas Chromatography Mass Spectrometry (GC-MS QP2010 Ultra). Based on the molecular weight and fragmentation patterns of the isolated compounds from the extract, a total of 9 active compounds were found in the 96% ethanol extract of *A. esculentus* with the primary component being 2(1H)-Pyridinone, Hydrazone, Dihydrochloride (CAS) at a concentration of 42.48% (Table 2). Figure 2 shows the chromatogram of 2(1H)-Pyridinone, Hydrazone, Dihydrochloride (CAS).

Table 2. GC-MS analysis of a 96% ethanol extract derived from green *A. esculentus*.

No	Compound Name	Retention Time (minutes)	Area	Concentration (%) w/v
1	*Imidazole*, 2-*Fluoro*-5-*Carbhydrazino*-1-*Methyl*-	9.966	6.887.404	14.50
2	2-*Chlorobenzyl* 2,2,2-*Trichloro*-1- (*P-Toluidino) Ethylcarbamate*	11.465	287.878	0.61
3	2,3′-*Bifuran*, 2,2′,3′,5-*Tetrahydro*- (CAS)	11.690	1.280.743	2.70
4	*Silane, Methylenebis [Trimethyl*- (CAS) 2,2,4,4-*Tetramethyl*-2,4-*Disilapentane*	12.524	2.171.800	4.57
5	2,3-*Dihydro*-3,2′-*Bis*-*Furan*	14.058	751.385	1.58
6	4-*Hydroxy*-3-*Methoxybenzylamine Hydrochloride*	15.345	1.303.049	2.74
7	2,3′-*Bifuran*, 2,2′,3′,5-*Tetrahydro*- (CAS)	16.203	6.206.044	13.06
8	2(1H)-*Pyridinone, Hydrazone, Dihydrochloride* (CAS)	16.696	20.181.622	42.48
9	2-(2-*Nitrovinyl*) *Furan*	16.880	8.434.150	17.75
	Total		47.504.075	100.0

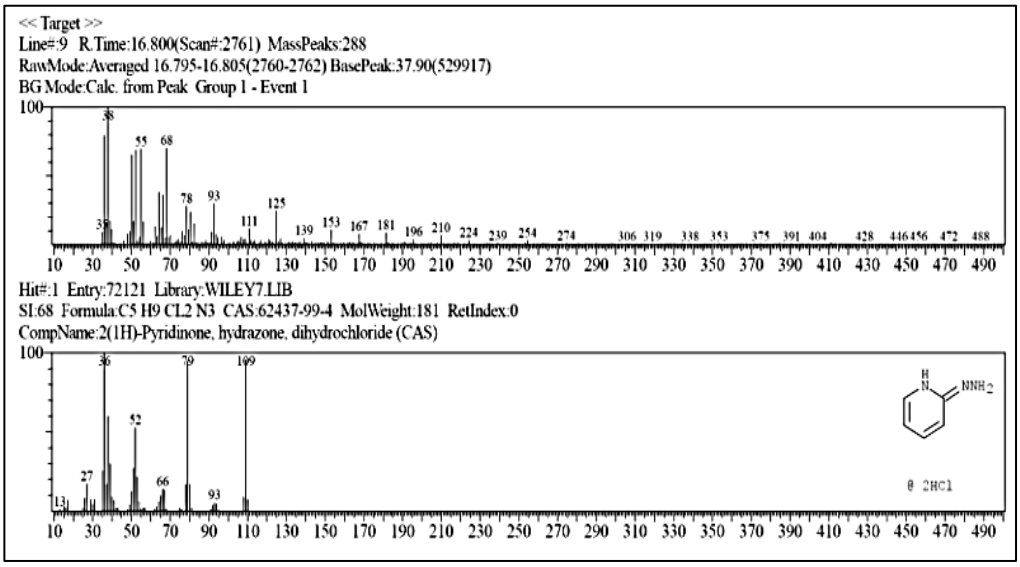

Figure 2. Chromatogram of 2(1H)-pyridinone, hydrazone, dihydrochloride (CAS)

The results of the antioxidant activity testing of the 96% ethanol extract from green *A. esculentus* using the DPPH method are presented in Table 2. The testing results indicate that the concentration of *A. esculentus* extract that successfully quenched DPPH by 50% is 169.09 ppm (Table 3).

Table 3. Antioxidant activity of green *A. esculentus* pods extract using DPPH method.

Concentration (ppm)	Absorbance	% DPPH Inhibition (IC_{50})
100	0.594	29.117
150	0.447	46.659
169.09	**0.419**	**50**
200	0.322	61.575
250	0.255	69.570
300	0.121	85.561

Note: concentration = 96% ethanol extract of *A. esculentus*; absorbance = measurement value of DPPH absorbance.

The pre-treatment blood glucose levels ranged from 172.50 ± 20.54 to 196.43 ± 34.52 mg/dL. Statistical analysis showed there was no significant difference among groups ($p>0.05$), thus demonstrates that the diabetic mice had relatively comparable baseline glycemic conditions before treatment. The mean body weights of mice in this study ranged from 26.36 ± 0.63 to 26.67 0.57 g.

Statistical analysis showed that all groups had no significant differences in body weight before treatment (P>0.05), so the animals had comparable baseline body weights and were homogeneous before treatment (Table 4).

Table 4. The blood glucose levels and body weight of mice before and after treatment.

Treatments	Blood Glucose Levels (mg/dL)		Body Weight (g)	
	Pre-treatment	Post-treatment	Pre-Treatment	Post-Treatment
K(-)	188.14 ± 15.93 ^{a}	174.29 ± 11.09 ^{b}	26.36 ± 0.63 ^{a}	27.66 ± 3.12 ^{a}
K(+)	196.43 ± 34.52 ^{a}	125.29 ± 25.65 ^{a}	26.58 ± 0.59 ^{a}	31.37 ± 1.92 ^{c}
P1	182.57 ± 17.21 ^{a}	141.29 ± 39.40 ^{ab}	26.49 ± 0.55 ^{a}	29.08 ± 2.31 ^{b}
P2	174.57 ± 25.88 ^{a}	131.29 ± 23.53 ^{a}	26.42 ± 0.61 ^{a}	29.16 ± 2.59 ^{b}
P3	172.50 ± 20.54 ^{a}	121.33 ± 15.81 ^{a}	26.67 ± 0.57 ^{a}	30.52 ± 2.40 ^{c}

Note: K(-) = distilled water, K(+) = metformin 500 mg, P1 = *A. esculentus* extract 200 mg/kg bw; P2 = *A. esculentus* extract 300 mg/kg bw; P3 = *A. esculentus* extract 400 mg/kg bw. The body weight values of the mice (mean ± SD) followed by different superscript letters indicate significant differences (P<0.05); and the same superscript letters indicate there was no significant differences (P>0.05).

After the treatment period, blood glucose levels decreased in all treatment groups compared with their pre-treatment values. The negative control group K(−) which received aquadest, exhibited the highest post-treatment blood glucose level (174.29 ± 11.09 mg/dL), still in the range of hyperglicemia. In contrast, the positive control group treated with metformin K(+) showed a significant decrease in blood glucose level to 125.29 ± 25.65 mg/dL. Among the groups treated with the 96% ethanol extract of *A. esculentus*, blood glucose levels after treatment were 141.29 ± 39.40, 131.29 ± 23.53, and 121.33 ± 15.81 mg/dL (P1, P2, and P3, respectively). Statistical analysis revealed significant differences in post-treatment blood glucose levels among treatment groups (P<0.05).

After the treatment period, body weight differed significantly among the experimental groups. The negative control group (K−) had the lowest mean body weight (27.66 ± 3.12 g), whereas the positive control (K+) and the highest-dose *A. esculentus* extract group (P3) exhibited the highest body weights (31.37 ± 1.92 and 30.52 ± 2.40 g, respectively) and did not differ significantly (P>0.05). The P1 and P2 groups showed intermediate body weights (29.08 ± 2.31 and 29.16 ± 2.59 g, respectively), with no significant difference between them but significantly lower values than K(+) and P3. Overall, administration of the 96% ethanol extract of *A. esculentus* increased body weight in a dose-dependent manner, with the highest dose (400 mg/kg body weight) producing an effect comparable to that of metformin.

Statistical analysis showed that the administration of ethanol extract of 96% *A. esculentus* affects the diameter of the island of Langerhans and its histological structure. The K(−), K(+), and P1 groups had the diameters of Langerhans islands of 20.90 ± 1.59, 19.05 ± 2.85, and 25.02 ± 1.15 µm, respectively, which were not statistically significant. In contrast, the P2 (43.29 ± 5.63 µm) and P3 (36.90 ± 4.33 µm) groups showed larger diameters and were significantly different from K(−), K(+), and P1. Diameter of Islets of Langerhans are shown in Table 5, while visual representatives are presented in Figure 3.

Table 5. Diameter of islets of Langerhans in the pancreas after treatment.

Treatments	Diameter of Langerhans Islets in the pancreas (µm)
K(-)	20.90 ± 1.59^{a}
K(+)	19.05 ± 2.85^{a}
P1	25.02 ± 1.15^{a}
P2	43.29 ± 5.63^{b}
P3	36.90 ± 4.33^{b}

Note: Diabetic mice K(-) = distilled water, K(+) = metformin 500 mg, P1 = *A. esculentus* extract 200 mg/kg bw; P2 = *A. esculentus* extract 300 mg/kg bw; P3 = *A. esculentus* extract 400 mg/kg bw. The values are expressed as mean ± SD. Significant differences within the same column are indicated by different superscript letters (P<0.05).

DISCUSSION

The 96% ethanol extract of green *A. esculentus* contains secondary metabolites, including alkaloids, steroids, phenolics, saponins, flavonoids, and tannins (Table 1). Secondary metabolites in plants that served as antioxidants included flavonoids, phenolics, tannins, and saponins (Happy et al., 2025). In this research, the highest metabolite among the nine active compounds identified in the 96% ethanol extract of green *A. esculentus* pods was 2-(1)-Pyridinone Hydrazone Dihydrochloride (CAS), which accounted for 42.48%. This active compound corresponded to the eighth absorption peak, with a retention time of 16.696 minutes (Table 2). It belonged to the alkaloid class of a pyridine core structure

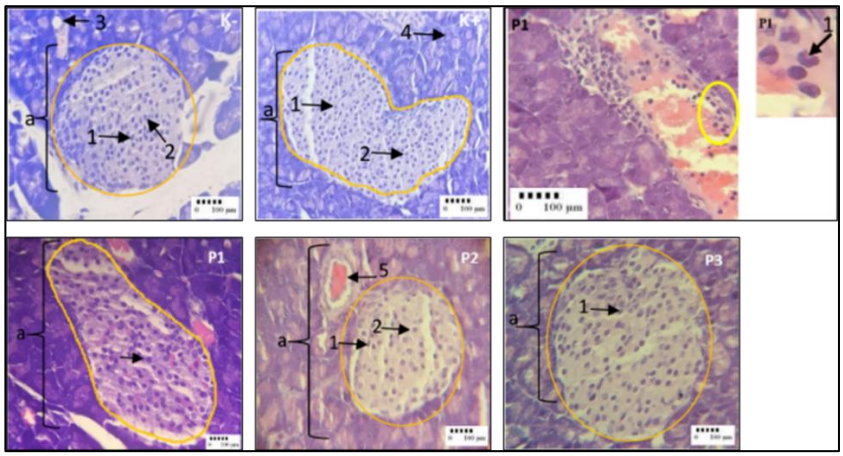

Figure 3. Histology of the pancreatic islets of Langerhans in mice. Note: K(-) = distilled water, K(+) = metformin 500 mg, P1 = *A. esculentus* extract 200 mg/kg bw; P2 = *A. esculentus* extract 300 mg/kg bw; P3 = *A. esculentus* extract 400 mg/kg bw; yellow circle = islet of Langerhans; 1= α cells (irregular nucleus); 2= β cells (large and round nucleus); 3= intralobular duct; 4= pancreatic acini; 5= blood vessels (staining with Hematoxylin and Eosin, magnification 400x, scale bar 100µm).

and had a chemical formula of $C_5H_9C_{l2}N$. The highest metabolite content in this study contrasted with the findings of El-Hagrassi et al. (2019), which reported 9,12-octadecadienoic acid, methyl ester $C_{19}H_{34}O_2$ at 13.54% and the dominant 3,4-dimethoxybenzoic acid at 21.82%.

The potential of crude extract from *A. esculentus* pods in this research as an antioxidant was evaluated by examining the IC_{50} value. The IC_{50} value of *A. esculentus* extract was 169 ppm (Table 3), indicated weak antioxidant activity. The IC_{50} value was inversely related to antioxidant activity; as antioxidant activity increased, the IC_{50} value decreased. Compared to the antioxidant activity of ethanol extract from *A. esculentus* leaves reported by Delviana (2017), the IC_{50} of *A. esculentus* pods was lower. The antioxidant activity of ethanol extract from *A. esculentus* leaves was classified as strong, with an IC_{50} value of 75.68 ppm. According to Zuhdi et al. (2019), the age at harvest influenced the antioxidant activity of *A. esculentus*, where prolonged harvest age tended to enhance antioxidant activity.

The main parameter of this study was changes in blood glucose levels before and after treatment (Table 4). The negative control group differed significantly from the positive control and extract-treated groups. However, the positive control and the higher-dose extract groups showed comparable glycemic responses. The treatment with *A. esculentus* extract reduced blood glucose levels in diabetic mice, with higher doses showed better antihyperglycemic effects. When compared with the normal reference value for mice (<125 mg/dL), only the P3 group (121.33 ± 15.81 mg/dL) reached the normal glycemic range, while the K(+) group (125.29 ± 25.65 mg/dL) approached the threshold. In contrast, the K(−), P1, and P2 groups remained above the normal limit. Although glucose levels decreased substantially, complete normalization had not yet been achieved in these groups.

Normal fasting blood glucose levels in mice were generally comparable to those in humans, although not identical, typically ranged between 70–120 mg/dL pdepending on strain and experimental conditions, while values below 125 mg/dL were commonly used as a reference threshold for normoglycemia (Benedé-Ubieto et al., 2020; American Diabetes Association, 2022). The highest extract dose (400 mg/kg body weight) group resulted in final blood glucose levels that were closest to normal conditions (<125 mg/dL). These results are consistent with the mechanism that the secondary metabolite of *A. esculentus* increases the utilization of glucose by tissues and reducing hyperglycemia.

In this study, the weight of the mice before treatment did not differ significantly between groups so that all test animals had homogeneous initial conditions. After treatment, the negative control group showed the lowest body weight, while the positive control group (metformin) had the highest body weight. The group given 96% of *A. esculentus* ethanol extract experienced weight gain, and the 400 mg/kg weight loss dose resulted in the closest weight gain to the metformin group.

Hyperglycemia in Type 1 Diabetes Mellitus (T1DM) results from the destruction of pancreatic β-cells, leading to an absolute or near-absolute deficiency of insulin secretion. In alloxan-induced diabetes, excessive reactive oxygen species (ROS) generated within β-cells cause oxidative stress, cellular damage, and apoptosis, resulting in persistent hyperglycemia (Lenzen, 2008; Furman, 2021). The antihyperglycemic effect of the 96% ethanol extract of *A. esculentus* was therefore more likely related to its antioxidant and cytoprotective properties than to improvements in insulin sensitivity. Flavonoids

and polyphenols present in the extract can scavenge ROS, reduce oxidative damage, and preserve the viability of pancreatic β-cells, thereby maintaining endogenous insulin secretion (Peter et al., 2021).

This mechanism is supported by the histological findings, in which the P2 and P3 groups exhibited significantly larger islets of Langerhans and better-preserved islet architecture than the negative control group. Preservation of islet morphology indicates reduced β-cell damage and improved pancreatic endocrine function, which likely contributed to the observed reduction in blood glucose levels. Although the P2 group had a larger mean islet diameter than the P3 group, P3 achieved better glycemic control. This suggests that islet size alone does not determine β-cell function. Blood glucose regulation depends more on the viability and insulin-secreting capacity of β-cells than on islet morphology. Therefore, the greater antihyperglycemic effect observed in the P3 group may reflect better preservation of functional β-cells and endogenous insulin secretion, despite its slightly smaller islet diameter. Similar findings have shown that glycemic improvement is more closely related to functional β-cell preservation than to islet size alone (Eizirik et al., 2020; Weir and Bonner-Weir, 2013).

Oxidative stress is one of the main mechanisms of pancreatic damage in diabetes. Hyperglycemia increases the formation of reactive oxygen species (ROS) which then activates NF-κB, a transcription factor that increases the production of pro-inflammatory cytokines and accelerates tissue damage (Abedimanesh et al., 2022). On the other hand, the activation of Nuclear factor erythroid 2-related factor 2 (Nrf2) increases the expression of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) so that it is able to suppress oxidative stress. Nrf2 is currently seen as an important target in diabetes therapy (Triana et al., 2023). Many phytochemicals, particularly flavonoids and polyphenols, are known to activate the AMPK/SIRT1 pathway which further inhibits NF-κB activation resulting in decreased inflammation and reduced tissue damage (Abedimanesh et al., 2022). Improvement in pancreatic histology in the *A. esculentus* extract treatment group is likely a consequence of reduced oxidative and inflammatory stress due to the antioxidant activity of secondary metabolites of *A. esculentus* pods.

Flavonoids and polyphenols are able to decrease β cell apoptosis, increase β cell proliferation, increase insulin gene expression, maintain the secretory function of the pancreas, improve the size and integrity of the island of Langerhans (Uti et al., 2025). In this study, the diameter of the Langerhans island increased in the treatment group, especially P2 and P3, with a more regular cell arrangement than the controls. In contrast, the control group showed a smaller diameter. These findings support the hypothesis that *A. esculentus* pods ethanol extract exerts a cytoprotective effect on pancreatic β cells so that insulin secretion capacity can be maintained or improved.

CONCLUSION

The 96% ethanol extract of green okra pods (*Abelmoschus esculentus* L.) contains chemical compounds belonging to the flavonoid and alkaloid groups. The predominant active compound identified was 2(1H)-Pyridinone, Hydrazone, Dihydrochloride (CAS). The extract has potential as an antidiabetic agent in hyperglycemic-induced mice (*Mus musculus* L.), demonstrated by its ability to lower blood glucose levels, increase body weight, and improve the histological structure of the islet of Langerhans pancreas. An extract dose of 300 mg/kgBB showed the best effectiveness in improving the histological structure of the pancreas, while a dose of 400 mg/kgBB provided a reduction in blood glucose levels that was closest to normal.

ACKNOWLEDGEMENTS

The authors would like to thank I Gede Wiranatha for supporting the animal handling and data sampling during the research.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

Abedimanesh N, Nouri M, Mohammadnejad K, Barati M, Dabardani E, Kakavand E, Eskandari MR, Hosseini SH, Mohammadi M, Anarkooli IJ, Noubarani M, Andalib S, Yazdinezhad A and Motlagh B, 2022. *Vinca herbacea* extract suppresses NF-kB signaling and modulates SIRT1/AMPK/PGC1α axis to exert antidiabetic effects in streptozotocin-induced diabetic rats. *Research Journal of Pharmacognosy* 9(1): 1–15.

American Diabetes Association, 2022. Standards of medical care in diabetes—2022 abridged for primary care providers. *Clinical Diabetes* 40(1): 10–38.

Anjani PP, Damayanthi E, Rimbawan R and Handharyani E, 2018. Antidiabetic potential of purple okra (*Abelmoschus esculentus* L.) extract in streptozotocin-induced diabetic rats. *IOP Conference Series: Earth and Environmental Science* 196: 012038.

Astati and Kasmawati, 2017. Pengaruh tepung okra terhadap berat badan tikus Wistar diabetes. *Jurnal Sains dan Teknologi Pangan* 2(1): 335–341.

Bell KJ and Lain SJ, 2025. The changing epidemiology of Type 1 diabetes: A global perspective. *Diabetes, Obesity and Metabolism* 27(Suppl 6): 3–14.

Benedé-Ubieto R, Estévez-Vázquez O, Ramadori P, Cubero FJ and Nevzorova YA, 2020. Guidelines and considerations for metabolic tolerance tests in mice. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy* 13: 439–450.

Delviana, 2017. Aktivitas antioksidan dari ekstrak etanol daun okra (*Abelmoschus esculentus* Moench). *Skripsi*. Universitas Sumatera Utara, Fakultas Farmasi, Program Studi Sarjana Farmasi.

El-Hagrassi AM, Osman AF, El-Manawaty MA, Eskander DM and Nassar MI, 2019. Characterization and biological evaluation of the isolated phenolic constituents of *Urginea maritima* (L.) aerial parts. *Bioscience Research* 16(1): 720–732.

Ermayanti NGAM, Suaskara IBM, Widhyastini IGAM and Setyawati I, 2023. Blood glucose level and pancreas histological section of male rabbits after being fed commercial feed supplemented with cod liver oil. *Sains Natural: Journal of Biology and Chemistry* 13(1): 39–46.

Eizirik DL, Pasquali L and Cnop M, 2020. Pancreatic β-cells in Type 1 and Type 2 diabetes mellitus: Different pathways to failure. *Nature Reviews Endocrinology* 16(7): 349–362.

Furman BL, 2021. Streptozotocin-induced diabetic models in mice and rats. *Current Protocols* 1(4): e78.

Happy TA, Septiani L, Graharti R and Andrifianie F, 2025. The potential of secondary metabolite compounds from Indonesian medicinal plants as antioxidant agents: A literature review. *Medical Profession Journal of Lampung* 15(3): 619–623.

Hughes DS and Narendran P, 2014. Alpha cell function in Type 1 diabetes. *British Journal of Diabetes and Vascular Disease* 14(2): 45–51.

Irshad M, Debnath B, Mitra S, Arafat Y, Li M, Sun Y and Qiu D, 2018. Accumulation of anthocyanin in callus cultures of red-pod okra [*Abelmoschus esculentus* (L.) Hongjiao] in response to light and nitrogen levels. *Plant Cell, Tissue and Organ Culture* 134(1): 29–39.

Lenzen S, 2008. The mechanisms of alloxan- and streptozotocin-induced diabetes. *Diabetologia* 51(2): 216–226.

Nortjie E, Basitere M, Moyo D and Nyamukamba P, 2022. Extraction methods, quantitative and qualitative phytochemical screening of medicinal plants for antimicrobial textiles: A review. *Plants* 11(15): 2011.

Molyneux P, 2004. The use of the stable free radical diphenylpicrylhydrazyl (DPPH) for estimating antioxidant activity. *Songklanakarin Journal of Science and Technology* 26(2): 211–219.

Peter EL, Nagendrappa PB, Ajayi CO and Sesaazi CD, 2021. Total polyphenols and antihyperglycemic activity of aqueous fruits extract of Abelmoschus esculentus: Modeling and optimization of extraction conditions. *PLOS ONE* 16(4): e0250405.

Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V and Orekhov AN, 2020. The diabetes mellitus–atherosclerosis connection: The role of lipid and glucose metabolism and chronic inflammation. *International Journal of Molecular Sciences* 21(5): 1835.

Setyawati I, 2019. Histology of rat pancreas treated with Calliandra calothyrsus leaf in the diets during pregnancy and lactation. *Advances in Tropical Biodiversity and Environmental Sciences* 3(1): 1–7.

Sims EK, Mirmira RG and Evans-Molina C, 2020. The role of beta cell dysfunction in early Type 1 diabetes. *Current Opinion in Endocrinology, Diabetes and Obesity* 27(4): 215–224.

Sherif IO and Al-Gayyar MM, 2013. Antioxidant, anti-inflammatory, and hepatoprotective effects of silymarin on hepatic dysfunction induced by sodium nitrite. *European Cytokine Network* 24(3): 114–121.

Triana R, Sukmawati IR, Syamsunarno MRAA and Lestari K, 2023. Higher Nrf2 level is correlated with metabolic parameters in Type 2 diabetes mellitus. *Indonesian Biomedical Journal* 15(6): 383–390.

Utami RP, 2018. Kandungan gizi, total fenol, kuersetin, dan kapasitas antioksidan total pada berbagai proses pemasakan okra (*Abelmoschus esculentus* L.). *Tesis*. Institut Pertanian Bogor, Bogor.

Uti DE, Atangwho IJ, Alum EU, Egba SI, Okechukwu UPC and Ikechukwu GC, 2025. Natural antidiabetic agents: Current evidence and development pathways from medicinal plants to clinical use. *Natural Product Communications* 20(3).

Wahyuningsih SPA, Pramudya M, Putri IP, Savira NII, Winarni D, Suhargo L and Darmanto W, 2017. Okra polysaccharides improve spleen weight and B-lymphocytes proliferation in mice infected by Staphylococcus aureus. *Biosaintifika* 9(3): 460–465.

Wardani G, Farida N, Andayani R, Kundiri M and Sudjarwo SA, 2017. The potency of red seaweed (*Eucheuma cottonii*) extracts as hepatoprotector on lead acetate-induced hepatotoxicity in mice. *Pharmacognosy Research* 9(3): 282–286.

Weir GC and Bonner-Weir S, 2013. Islet β cell mass in diabetes and how it relates to function, birth, and death. *Annals of the New York Academy of Sciences* 1281: 92–105.

Zuhdi MF, Sinar S and Achmad D, 2019. Pengaruh umur panen terhadap aktivitas antioksidan dan kualitas buah okra merah (*Abelmoschus esculentus* L. Moench). *Skripsi*. Universitas Trunojoyo Madura, Madura.