JTL 13 (2) December 2024
Page: 145-155
Contents list available at Jurnal Teknologi Laboratorium
JURNAL TEKNOLOGI LABORATORIUM
Journal Homepage: www.teknolabjournal.com
ISSN 2580-0191(Online) I ISSN 2338 – 5634(Print)

Original Research

Effect of Sechium edule extract on blood sugar levels and pancreatic histopathology in male Rats with type II diabetes mellitus

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Abstract: Diabetes mellitus (DM) is a metabolic disorder characterized by elevated blood glucose levels (hyperglycemia) and the presence of glucose in the urine (glucosuria). The etiology of diabetes varies depending on its type, including Type 1 diabetes, which is caused by autoimmune destruction of pancreatic beta cells responsible for insulin production; Type 2 diabetes, resulting from insulin resistance; and gestational diabetes, triggered by hormonal changes during pregnancy affecting insulin sensitivity. Insulin plays a crucial role in glucose metabolism by converting glucose into glycogen for storage. This study aimed to evaluate the effect of Siamese pumpkin extract (Sechium edule) on blood glucose levels in male Wistar rats (Rattus norvegicus) with type II diabetes. A pre-test and post-test control group experimental design was employed, using 25 rats divided into five groups: a negative control group, a positive control group, and treatment groups receiving chayote extract at doses of 14 mg/kgBW, 28 mg/kgBW, and 42 mg/kgBW, respectively. Streptozotocin (STZ) was administered to induce diabetes in all groups except the negative control. Data analysis included normality tests, homogeneity tests, ANOVA, and post-hoc multiple comparison tests. The results demonstrated that Siamese pumpkin extract contains active compounds such as alkaloids, saponins, flavonoids, steroids, triterpenoids, tannins, and glycosides. Among the treatment groups, the administration of chayote extract at a dose of 42 mg/kgBW resulted in the most significant reduction in blood glucose levels compared to the lower doses. Histopathological analysis of pancreatic tissue revealed no abnormalities, necrosis, or degeneration across all treatment groups. The superior efficacy of the 42 mg/kgBW dose is attributed to the higher concentration of active compounds, enhanced glucose-lowering mechanisms, and improved systemic distribution.

Keywords: Type II Diabetes Mellitus; Blood Sugar Level; Pancreatic Histopathology; Siamese Pumpkin Extract.

INTRODUCTION

Diabetes mellitus (DM) is a disorder of carbohydrate metabolism characterized by elevated blood glucose levels (hyperglycemia) and the presence of glucose in urine (glucosuria). Hyperglycemia negatively impacts overall health by promoting the formation of free radicals or reactive oxygen species through oxidative-reduction mechanisms, which increase electron donors in the mitochondrial electron transport chain[1]. This metabolic imbalance can impair pancreatic beta-cell function, resulting in inadequate insulin production or insulin resistance, both of which contribute to hyperglycemia[2]. In such cases, glucose accumulates in the bloodstream without being utilized by cells due to resistance at insulin receptor sites[3]. DM is broadly classified into type 1, characterized by autoimmune destruction of pancreatic beta cells, and type 2, which is associated

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DOI: 10.29238/teknolabjournal.v13i2.499
Received 25 June 2024; Received in revised form 21 October 2024; Accepted 10 December 2024

with insulin resistance, peripheral tissue dysfunction, and beta-cell insufficiency[4]. I

n Indonesia, diabetes is a significant health challenge marked by chronic hyperglycemia and metabolic disturbances in carbohydrates, fats, and proteins[5]. As of 2023, the World Health Organization (WHO) estimates that more than 422 million people worldwide suffer from diabetes, which caused 1.5 million deaths in 2019[6]. Globally, diabetes prevalence is approximately 28.3% in Pakistan, 10% in the United States, and 8.5% among Indonesians aged ≥15 years[7]. In Medan, Indonesia, the Basic Health Research (RISKESDA) report of 2018 noted a prevalence of 58.73%[8]. Type 2 diabetes mellitus poses a serious threat to developing nations like Indonesia, where 80% of cases occur in low- and middle-income regions[9].

Type 2 diabetes mellitus poses a serious threat to developing nations like Indonesia, where 80% of cases occur in low- and middle-income regions[10]. Such complications are influenced by genetic, environmental, and lifestyle factors, as well as delays in diagnosis and treatment[11]. The underlying mechanism involves vascular dysfunction due to oxidative stress, which damages endothelial cells and other tissues unable to regulate glucose transport[12].

Modifiable risk factors for diabetes include poor dietary habits, smoking, obesity, hypertension, stress, lack of physical activity, and alcohol consumption[13]. While diabetes prevalence is similar between genders, women may be at slightly higher risk due to physiological factors such as pregnancy-related weight gain, higher life expectancy, and greater prevalence of obesity and hypertension[14].

Patient non-adherence to pharmacological treatments often exacerbates diabetes, prompting interest in alternative therapies using phytopharmaceuticals. These plant-based treatments are considered cost-effective, widely available, and associated with fewer side effects[15]. One such plant, chayote (Sechium edule), is traditionally used for medicinal purposes. Belonging to the Cucurbitaceae family, chayote is a nutrient-rich fruit commonly consumed as a vegetable or in herbal preparations[16].

Chayote exhibits a range of biological activities, including antioxidant, antimicrobial, diuretic, antihypertensive, and hypocholesterolemic effects[17]. Its active compounds include flavonoids, alkaloids, and saponins, which are known to support cardiovascular health[18]. Additionally, its potassium content may enhance its hypoglycemic potential[19]. This study investigates the anti-diabetic efficacy of chayote extract in male Wistar rats (Rattus norvegicus) induced with streptozotocin (STZ), focusing on its glucose-lowering effects and histopathological impact on pancreatic tissue. Unlike prior studies, this research aims to elucidate the optimal dosage of chayote extract for therapeutic use, thereby providing a approach to diabetes management.

MATERIAL AND METHOD

This study employed a pre-test and post-test only control group experimental design[20]. The research was conducted at the Pharmacology Laboratory of the Faculty of Pharmacy, University of North Sumatra, and the Anatomical Pathology Laboratory of the Royal Prima Medan Hospital from January to April 2024. Ethical approval was obtained from the Prima Indonesia University Health Research Ethics Committee (034/KEPK/UNPRI/XII/2023).

Experimental Design

The study utilized 25 male Wistar rats (Rattus norvegicus), randomly divided into five groups (five rats per group) to evaluate the effect of chayote extract on blood glucose levels. The groups were as follows:

1. **Negative Control (K-)**: No streptozotocin (STZ) induction or chayote extract treatment.
2. **Positive Control (K+)**: Induced with STZ (45 mg/kg body weight) but no chayote extract treatment.

3. **Treatment 1 (P1)**: Induced with STZ (45 mg/kg body weight) and administered chayote extract (14 mg/kg body weight).
4. **Treatment 2 (P2)**: Induced with STZ and administered chayote extract (28 mg/kg body weight).
5. **Treatment 3 (P3)**: Induced with STZ and administered chayote extract (42 mg/kg body weight).

The rats were acclimatized for one week before the study. On day 0, fasting blood glucose levels were measured. Rats in the treatment and positive control groups were fasted for 8 hours before receiving STZ induction via intraperitoneal injection (45 mg/kg body weight dissolved in 0.9% NaCl). Hyperglycemia was confirmed 3 days post-induction (fasting blood glucose levels between 200–349 mg/dL)[21]. Chayote extract was administered orally every morning for 4 weeks. The negative control and treatment groups of rats (rattus wistar strain) were given swimming exercises for 20 minutes, the treatment was given every 3 times a week and lasted for 4 weeks[22].

Preparation of Chayote Extract

Chayote (Sechium edule) was extracted using the maceration method. Fresh chayote was processed with 95% ethanol for 72 hours, followed by an additional 48-hour maceration. The filtrate was concentrated using a rotary evaporator to obtain a thick ethanol extract[23].

FTIR (Fourier Transform Infrared) screening

FTIR can be used quantitatively because it can determine a compound in a sample. through at a particular wavelength is directly proportional to the amount of kinetic energy associated[24].

Phytochemical Screening

Qualitative tests were performed to identify secondary metabolites, including alkaloids, flavonoids, saponins, and tannins in the ethanol extract of chayote[16].

Induction of Diabetes

Streptozotocin (STZ) was prepared at a dose of 45 mg/kg body weight, dissolved in 0.9% NaCl. Following STZ induction, rats were provided 1% glucose solution to prevent hypoglycemia[25]. Hyperglycemia was confirmed on the third day using a glucometer.

Histopathological Preparation

Pancreatic tissue was collected and fixed in 10% formalin[26]. The tissue was processed through stages of dehydration, clearing, embedding in paraffin, and sectioning into 2 µm slices[27]. Hematoxylin and eosin (H&E) staining was performed, and slides were observed under a light microscope for histopathological changes such as inflammation, necrosis, or degeneration[26,27].

Statistical Analysis

Data were analyzed using one-way ANOVA ($p \leq 0.05$) after confirming normality (Shapiro-Wilk test, $p > 0.05$) and homogeneity (Levene's test, $p > 0.05$). Post hoc Mann-Whitney tests were applied to determine differences between groups[28,29].

RESULTS AND DISCUSSION

Phytochemical Screening

The results of the phytochemical screening test on the 96% ethanol extract of chayote were observed and determined based on the reactions formed with specific reagents.

Table 1. Phytochemical Screening Results of 96% Ethanol Extract of Chayote (Sechium edule)

Compound Group	Test Reagents	Result
Alkaloids	Bouchardat	Positive
	Mayer	Positive
	Dragendorff	Positive
Terpenoids/Steroids	Salkowski	Positive
	Liebermann-Burchard	Positive

Saponins	Distilled water + 96% ethanol	Positive
Flavonoids	Magnesium (Mg) + HCl	Positive
Tannins	1% Ferric chloride ($FeCl_3$)	Positive
Glycosides	Molisch	Positive

Table 1 shows the results of the phytochemical test of the chemical components of chayote fruit show that chayote extract contains alkaloids, terponoids/steroids, saponins, flavonoids, tannins, glycosides. The table provides an overview of the secondary metabolite compounds detected in the study, along with the reagents used for qualitative analysis and their respective results. The presence of alkaloids was confirmed through tests with Bouchardat, Mayer, and Dragendorff reagents, all yielding positive results, which indicates a significant presence of these compounds. Terpenoids and steroids were also detected using the Salkowski and Liebermann-Burchard reagents, both showing positive outcomes that confirm their presence.

Saponins were identified using a mixture of distilled water (aquadest) and 96% alcohol, with the test producing a positive result, highlighting the presence of these bioactive compounds. Similarly, flavonoids were confirmed using a combination of magnesium (Mg) and hydrochloric acid (HCl), as evidenced by a positive reaction. The presence of tannins was verified through a test with 1% ferric chloride ($FeCl_3$), which yielded a positive outcome. Lastly, glycosides were detected using Molisch's test, as shown by the positive result.

Overall, the results indicate that the tested extract contains a diverse range of secondary metabolite compounds, including alkaloids, terpenoids/steroids, saponins, flavonoids, tannins, and glycosides. These findings underscore the potential bioactivity and therapeutic properties of the extract.

FTIR Test Results of 96% Ethanol Extract of Siamese Pumpkin

The results of the FTIR test of 96% chayote ethanol extract to determine the functional groups contained in the sample can be observed in the figure below:

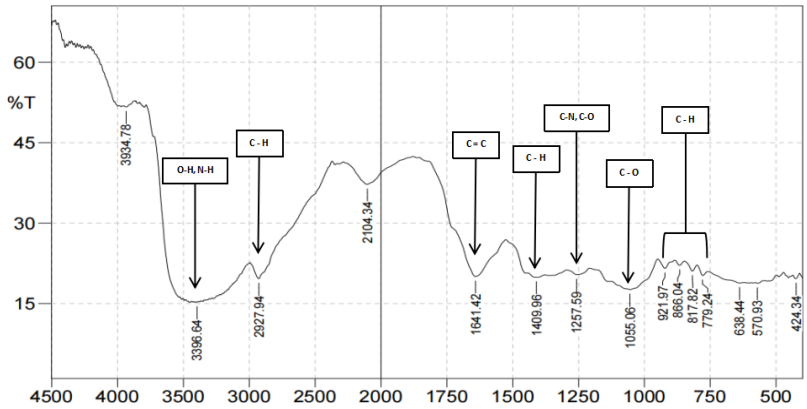

Figure 1. FTIR Test Results of Siamese Pumpkin Extract

The FTIR spectrum of the sample, presumably chayote (Sechium edule) extract, reveals the presence of several functional groups that are characteristic of bioactive compounds. A broad absorption peak observed at 3369.78 cm^{-1} corresponds to O-H stretching vibrations, indicating the presence of hydroxyl groups commonly found in alcohols and phenolic compounds. Additionally, this peak also reflects N-H stretching, which suggests the presence of amines or amides. A distinct peak at 2927.94 cm^{-1} is attributed to C-H stretching, characteristic of aliphatic hydrocarbons. A minor absorption at 2104.34 cm^{-1} indicates the potential presence of triple bonds, such as C≡C or C≡N, although this feature is less pronounced. The peak at 1641.42 cm^{-1} corresponds to C=C stretching, indicative of alkenes or aromatic compounds, while the absorption at 1409.95 cm^{-1} reflects C-H bending vibrations, likely associated with methyl or

methylene groups. Another significant feature is the band at 1257.56 cm^{-1}, attributed to C-N stretching, which suggests the presence of amines or amide functional groups. The strong absorption at 1055.06 cm^{-1} corresponds to C-O stretching, indicative of alcohols, esters, or ethers. In the fingerprint region (below 1000 cm^{-1}), peaks such as 783.22 cm^{-1} and 424.34 cm^{-1} represent C-H bending in aromatic or substituted compounds, providing structural specificity to the sample.

Figure 1 shows at wave numbers 779.24 cm1, 817.82 cm1, 866.04 cm1 and 921.97 cm1 indicate the presence of strong alkene and aromatic C-H functional groups. Strong C-H functional groups of alkane compounds are also present at wave numbers 1409.96 cm1, and 2927.94 cm1. At wave number 1257.59 cm1 shows the presence of C-N functional groups of amine compounds, amides and C=O functional groups of strong alcohol, ether, carboxylic acid and ester compounds. At wave number 1641.42 cm1, it shows the presence of C=C functional group of alkenes compound which changes. O-H functional groups of phenol compounds, nomoner alcohols and hydrogen bond alcohols are changing, sometimes widening and also the presence of N-H functional groups of amine and amide compounds which are present at wave number 3396.64 cm1. Overall, the FTIR spectrum confirms the presence of diverse functional groups, including hydroxyl, aliphatic hydrocarbons, amines, esters, and aromatic compounds. These findings align with the phytochemical composition of the extract, supporting the presence of secondary metabolites such as flavonoids, alkaloids, tannins, and saponins, which contribute to its bioactive properties.

Blood Sugar Level Measurement Results

Table 2 shows that in group K + treatment with STZ the average blood sugar level value is 0.26mg/dl. In group K- with treatment not given STZ and chayote extract, the average blood sugar level value is 0.00mg/dl. In group F1 with treatment given STZ and chayote extract, the average blood sugar level value is 0.47mg/dl. In group F2 with treatment given STZ and chayote extract, the average value of blood dula level is 0.54mg/dl. In group F3 with treatment given STZ and chayote extract, the average value of blood dula level is 0.61mg/dl.

The table presents data on the changes in blood glucose levels of rats (Rattus norvegicus) over time across five groups: Positive Control (K+), Negative Control (K-), and three treatment groups (F1, F2, F3). Each group contains three test subjects, and glucose levels were recorded at various time points (H1, H3, H6, H9, H12, H15, H18, H21, H24, H28), representing hours or days of observation.

The K+ group shows a minimal average reduction in glucose levels (0.26%), while the K- group exhibits no significant reduction (0.00%), indicating the absence of treatment effects in these groups. In contrast, the treatment groups (F1, F2, and F3) demonstrate progressively greater percentages of blood glucose reduction. F1 shows an average reduction of 0.47%, F2 achieves 0.54%, and F3 exhibits the highest reduction of 0.61%. This trend suggests a dose-dependent effect of the administered chayote extract, with F3 being the most effective in lowering blood glucose levels. The data underline the potential of chayote extract as a hypoglycemic agent, with its effectiveness increasing at higher doses. The controlled experimental design, including positive and negative controls, ensures the reliability of the results and highlights the therapeutic potential of chayote extract for managing diabetes.

Table 2. Blood sugar level measurement results

Group	K+			K-			F1			F2			F3		
Rat	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**
H1	465	496	547	82	80	90	283	307	585	342	561	578	478	549	563
H3	469	490	532	80	82	88	274	303	554	318	532	563	444	511	533
H6	460	485	530	81	84	91	261	295	534	307	510	531	418	467	510
H9	453	472	526	83	81	90	238	277	496	278	463	493	374	443	457
H12	433	453	505	78	84	93	221	258	458	244	448	451	344	407	411
H15	426	438	493	80	80	92	203	237	415	218	429	406	312	373	393
H18	407	419	475	79	78	90	190	226	375	196	388	378	276	321	354
H21	386	405	441	78	82	88	179	217	335	179	334	347	235	278	322
H24	367	382	413	79	80	89	166	201	285	162	285	321	207	245	296
H28	349	367	405	80	81	90	151	189	254	149	248	297	163	211	253
Percent Decrease	**0.25**	**0.26**	**0.26**	**0.02**	**0.01**	**0.00**	**0.47**	**0.38**	**0.57**	**0.56**	**0.56**	**0.49**	**0.66**	**0.62**	**0.55**
Average	**0.26**			**0.00**			**0.47**			**0.54**			**0.61**		

Table 3. Mean blood glucose levels and statistical comparisons among experimental groups

Group	Mean (mg/dL)	Standard Deviation (mg/dL)	Significance (P-Value) Compared to K+
Positive Control (K+)	458.07	40.61	-
Negative Control (K-)	112.76	91.67	0.000
14 mg/kgBW (F1)	287.46	92.28	0.001
28 mg/kgBW (F2)	361.86	97.33	0.234
42 mg/kgBW (F3)	373.83	104.75	0.456

The table 3 summarizes the mean blood glucose levels, standard deviations, and statistical comparisons among experimental groups to evaluate the effect of chayote extract on diabetic rats. The positive control group (K+) exhibited the highest mean blood glucose level (458.07 ± 40.61 mg/dL), while the negative control group (K-) had the lowest (112.76 ± 91.67 mg/dL). The treatment groups, receiving chayote extract at doses of 14 mg/kgBW (F1), 28 mg/kgBW (F2), and 42 mg/kgBW (F3), demonstrated intermediate reductions in glucose levels, with means of 287.46 ± 92.28, 361.86 ± 97.33, and 373.83 ± 104.75 mg/dL, respectively.

Statistical analysis using post hoc tests revealed significant differences ($P < 0.05$) between the positive control group (K+) and the treatment groups (F1 and F2), as well as between the negative control group (K-) and all other groups. However, no significant differences were observed between the treatment groups (F1 vs. F2, F2 vs. F3, or F1 vs. F3), indicating comparable hypoglycemic effects across the three doses of chayote extract. The lack of significant differences among treatment groups suggests a threshold effect where increasing the dose beyond 14 mg/kgBW does not result in proportionately greater glucose reduction.

Overall, the findings highlight the efficacy of chayote extract in lowering blood glucose levels, with significant improvements compared to the positive control group. These results suggest that chayote extract has potential as a natural therapeutic agent for diabetes management, with comparable effectiveness across the tested doses.

Histopathology of Pancreatic Wistar Male Rats

The use of chayote extract at a dose concentration of 42 mg/KgBB produced a length of Langerhans islets of 851.70 µm, wider than other doses.

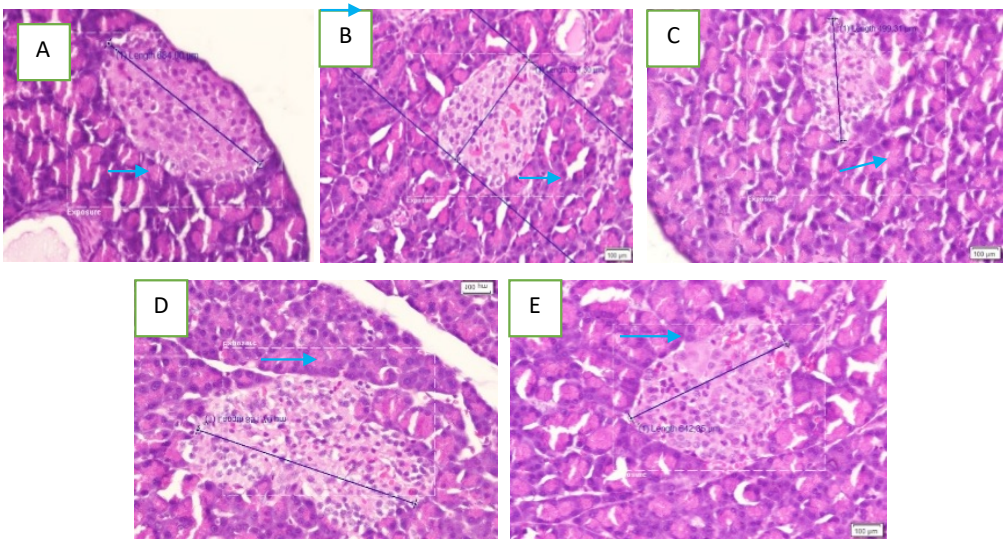

Figure 2. Histopathology of Pancreatic Wistar Male Rats

Figure 2 show the histopathology of the pancreas in male Wistar rats across different experimental groups. In the positive control group, the length of the islets of Langerhans was observed to be 684.00 µm. In the negative control group, the length of the islets of Langerhans measured 521.30 µm. The treatment group receiving a 14 mg/kgBW dose of chayote extract showed an islet length of 499.31 µm, while the group treated with a 28 mg/kgBW dose displayed the longest islet length at 851.70 µm. The 42 mg/kgBW dose group showed an islet length of 642.35 µm. Across all groups, no morphological abnormalities, necrosis, or degeneration were observed. Additionally, the exocrine glands of the pancreas remained intact, as indicated by the blue arrows.

Phytochemical analysis of chayote extract confirmed the presence of various active compounds, including alkaloids, flavonoids, steroidal saponins, triterpenoids, tannins, and glycosides. These compounds exhibit antioxidant and anti-inflammatory properties that inhibit carbohydrate absorption, enhance insulin sensitivity, and protect pancreatic beta cells, thereby accelerating diabetes recovery[30]. This activity contributes to lowering blood glucose levels by reducing the activity of key enzymes such as alpha-amylase and alpha-glucosidase, which are responsible for breaking carbohydrates into monosaccharides that can be absorbed by the intestine. Consequently, blood sugar levels remain stable[18].

The FTIR analysis further identified functional groups, such as ethers (C-O), associated with tannins and flavonoids in the chayote extract. Flavonoids, known for their antioxidant properties, can protect pancreatic beta cells from oxidative damage caused by reactive oxygen species[31]. Flavonoids also inhibit enzymes involved in carbohydrate metabolism and improve insulin sensitivity. Additionally, the potassium content in chayote stimulates insulin secretion, while niacin, a component of nicotinamide adenine dinucleotide (NAD), facilitates glycogenesis, further contributing to glucose reduction[7].

Chayote is a low-calorie food with a low glycemic index, rich in fiber, potassium, and bioactive compounds, making it beneficial for individuals with diabetes. Its high potassium-to-sodium ratio (62:1 per 100 grams) promotes heart and vascular health. Moreover, its high soluble fiber content slows carbohydrate digestion and absorption, preventing postprandial blood sugar spikes. Steamed chayote, with its filling starch content, serves as an alternative to excessive staple food consumption[7].

The one-way ANOVA test indicated that the hypoglycemic effect of chayote extract was most significant at a 42 mg/kgBW dose compared to 14 mg/kgBW and 28 mg/kgBW doses. This can be attributed to the higher concentrations of active compounds, such as flavonoids and alkaloids, at the highest dose. These compounds improve insulin sensitivity, reduce insulin resistance, and protect pancreatic beta cells. Secondary metabolites, particularly flavonoids, act as potent antioxidants that mitigate oxidative stress, prevent degenerative diseases such as diabetes, and restore insulin receptor sensitivity[32]. These findings underscore the potential of chayote extract as a natural therapy for diabetes management.

CONCLUSION

The study provides compelling evidence that chayote extract significantly reduces blood glucose levels, protects pancreatic tissue, and exhibits antioxidant properties that mitigate diabetes-induced oxidative stress. The findings underscore the potential of chayote as a natural adjunct therapy for diabetes management, with its multifaceted mechanisms of action contributing to glucose regulation and beta-cell protection. However, further clinical research is necessary to confirm its efficacy and safety in humans.

AUTHORS' CONTRIBUTIONS

Marti silfia prepared the samples, designed the protocols, executed the protocols, and wrote the manuscript. Gusbakti Rusip, Linda Chiuman reviewed and supervised the manuscript. All authors have read and approved the final manuscript.

ACKNOWLEDGEMENT

We would like to thank the Head of the Pharmacology Laboratory of the Faculty of Pharmacy, University of North Sumatra and the Head of the

Anatomical Pathology Laboratory of Royal Prima Medan Hospital, for all their support for this research.

FUNDING INFORMATION
This research is self-funding

DATA AVAILABILITY STATEMENT
The utilized data to contribute to this investigation are available from the corresponding author on reasonable request.

DISCLOSURE STATEMENT
The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors. The data is the result of the author's research and has never been published in other journals.

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