Trop J Nat Prod Res, July 2024; 8(7):7709-7714 ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Blood Glucose Lowering Effect of *Lagerstroemia speciosa* L. Leaves Extract on Type 2 Diabetic Rat Model

Dang X. Kien[1], Dinh V. Ha[2], Pham T. Kien[1], Truong H. A. Huy[1], Nguyen T. Nga[1], Vu M. Dung[1], Trinh D. Toan[1], Nguyen P. Anh[3,*], Nguyen H. Ngan[1,*]

[1]*Vietnam Military Medical University, 160 Phung Hung, Ha Dong, Hanoi, Vietnam*
[2]*Thien Duoc Technology Joint Stock Company, 24/74 Tu Hiep street, Thanh Tri, Hanoi, Vietnam*
[3]*Sarah Lawrence College, 1 Mead Way, Bronxville, NY 10708, USA*

ARTICLE INFO

Article history:
Received: 20 April 2024
Revised : 10 May 2024
Accepted: 02 June 2024
Published online 01 August 2024

ABSTRACT

Lagerstroemia speciosa (Lythraceae), commonly known as banaba, is a plant native to the tropical regions of Southeast Asia that thrives abundantly in Vietnam and has been historically utilized in traditional medicine. Despite evidence suggesting that its leaves have anti-diabetic properties, studies investigating the effects of *L. speciosa* extracts on animal models of type 2 diabetes remain limited. Herein, the effect of dry extract from *L. speciosa* leaves (VLDE) collected in Vietnam on blood glucose in type 2 diabetic rats was evaluated. White rats were divided into five groups, each comprising 10 rats. Group 1 served as the non-diabetic control, receiving distilled water, while type 2 diabetes was induced in other groups with a high-fat diet and low-dose streptozotocin. Group 3 received gliclazide at a dose of 20 mg/kg/day as the positive control, whereas groups 4 and 5 were administered VLDE at doses of 620 mg/kg/day and 1240 mg/kg/day, respectively, for a treatment duration of 28 days. Blood glucose levels, blood insulin levels, and insulin resistance indices were evaluated pre-and post-treatment. VLDE at both doses demonstrated significant blood glucose-lowering effects, accompanied by a reduction in the HOMA-IR index and elevation in the HOMA-*β*, QUICKI, and DI indices, as well as an increase in the pancreatic mass-to-body weight ratio, comparable to the gliclazide-treated group. Our findings underscore the potential of *L. speciosa* extract as a medicinal therapeutic agent for type 2 diabetes management, warranting further pre-clinical and clinical validation for pharmaceutical development.

Keywords: *Lagerstroemia speciosa*, banaba, type 2 diabetic, blood glucose lowering, *in vivo* test.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders globally and can be primarily attributed to two key factors: impaired insulin secretion by pancreatic β-cells and decreased insulin sensitivity of insulin-responsive tissues.[1] According to the International Diabetes Federation, 415 million individuals worldwide were affected by T2DM in 2015, with this number projected to rise to 642 million by 2040.[2] In Vietnam, it is estimated that one in every 20 individuals has T2DM, and the prevalence of prediabetes is three times as high.[3] T2DM increases the risk of macrovascular complications, such as heart failure and cardiovascular disease, microvascular complications, including lower limb amputations, retinopathy, and kidney failure, as well as hypoglycemic episodes and hyperglycemia.[4] Disease prevention, early detection, and effective blood glucose control are crucial for mitigating complications.[5]

*Corresponding author. Email: anguyen1@gm.slc.edu
Tel: +347-626-8576
nganvmu@gmail.com
Tel: +8438-268-9686

Citation: Kien DX, Ha DV, Kien PT, Huy THA, Nga NT, Dung VM, Toan TD, Anh NP, Ngan NH. Blood Glucose Lowering Effect of *Lagerstroemia speciosa* L. Leaves Extract on Type 2 Diabetic Rat Model. Trop J Nat Prod Res. 2024; 8(7): 7709-7714 https://doi.org/10.26538/tjnpr/v8i7.13

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Primary therapeutic approaches for T2DM involve pharmacological intervention combined with lifestyle changes. However, the long-term use of these pharmacotherapies often results in reduced treatment efficacy and the manifestation of numerous undesirable side effects.[6] Therefore, there is a pressing need for research to identify effective herbal products that lower blood glucose through various mechanisms to improve treatment efficacy and minimize the adverse effects of conventional pharmacological treatments.

Lagerstroemia speciosa (Lythraceae), commonly known as banaba, is a plant native to the tropical regions of Southeast Asia that thrives abundantly in Vietnam and holds an important tradition in folk medicine. Its leaves contain over 40 beneficial compounds, including corosolic acid, ellagitannins, and gallotannins, recognized for their contribution to blood sugar regulation.[7–9] Additionally, the leaves contain antioxidant phenols and flavonoids, including quercetin, gallic acid, and ellagic acid, which combat free oxygen radicals, provide anti-cancer effects and hepato-protection, and demonstrate antibacterial activities.[7,10–12] Corosolic acid, a pentacyclic triterpenoid derived from banaba leaves, demonstrates anti-diabetic, anti-inflammatory, and anti-tumor properties. It inhibits excessive proliferation and migration of pulmonary artery smooth muscle cells and downregulates the expression of signal transducer and activator of transcription 3 (STAT3).[13] The banaba leaf exhibits dual functions in treating diabetes and promoting weight loss by preventing carbohydrate accumulation and reducing adipogenesis.[14] Notably, silver nanoparticles fabricated from *L. speciosa* flower buds have been

reported to exert antimicrobial, anti-cancer, and apoptosis-promoting properties in the human osteosarcoma (MG-63) cell line.[15] In Vietnam, banaba grows abundantly in diverse *regions*, particularly in central provinces such as Nghe An, Ha Tinh, Thanh Hoa, Quang Tri, Quang Binh, Thua Thien Hue, Kon Tum, and Đak Lak. Despite its widespread growth, there is limited research exploring its effects on type 2 diabetes in animal models. Therefore, aiming to harness locally available herbal resources, this study seeks to evaluate the blood glucose-lowering effects of dry extracts from *L. speciosa* leaves (VLDE) on type 2 diabetes in white rats.

Materials and Methods

Materials

The dried leaves of banaba (*Lagerstroemia speciosa* L.) were harvested in August 2021 from Dong Hoi City, Quang Binh Province, Vietnam. Identification of the plant material was performed by Dr. Nguyen Quoc Binh of the Vietnam National Museum of Nature, Vietnam Academy of Science and Technology. A voucher specimen (No: QB0821) was deposited at the Laboratory of Pharmacology, Vietnam Military Medical University, to serve as a permanent reference. The dried leaf extract was prepared and supplied by Thien Duoc Technology Joint Stock Company (Hanoi, Vietnam). For evaluation of pharmacological effects, the dry powder was evenly dispersed in distilled water and administered to the rats using specialized curved gavage needles.

Extraction and Dosage Preparation

The dried banaba leaves were washed and desiccated until the moisture content reached less than 10%. The leaves were then ground into a powder and sieved through a 1 mm sieve to obtain a homogenous particle size. Five hundred grams of the powdered material were dissolved in 10 liters of reverse osmosis water and subjected to ultrasonic extraction for 60 minutes at 60 MHz and 60°C. The resulting extract was cooled to room temperature and filtered through sterile multi-layered gauze to remove impurities. Subsequently, the extract was concentrated under reduced pressure and dried using a spray dryer to yield a dried powder.

Folklore suggests a decoction of banaba leaves for diabetes treatment, with a dosage of 60-120 grams of dried material per person per day, translating to approximately 1-2 grams per kilogram body weight per day (assuming an average adult weight of 60 kg). The prepared dried extract of banaba leaves (VLDE) was obtained from the starting material at a 10:1 ratio (10 grams of dried leaves yielded 1 gram of dried extract). Based on this, the anticipated human dosage for VLDE would be 100-200 mg/kg/day. To convert this dose to an effective level for white rats, a conversion factor of 6.2 was applied as described in the study, resulting in two dosage levels for the animal experiments: 620 mg/kg/day and 1240 mg/kg/day.[16,17]

Equipment

The insulin resistance indices were measured using a Biochemical Systems International Srl Model 3000 Evolution biochemical analyzer (Italy). Blood glucose levels were determined with test strips and a OneTouch Profile Meter reader, both manufactured by Johnson & Johnson (USA). A 96-well plate reader from Thermo Fisher Scientific (Finland) was employed, and a Universal 320 refrigerated centrifuge from Hettich (Germany) was used.

Animals

The Wistar rats, weighing 200 ± 20 g, were obtained from the Animal Department of the Military Medical Academy. The rats were housed under standard laboratory conditions for a 10-day acclimation period before the commencement of the experiments. The experimental protocol was approved by the Vietnam Military Medical University, Hanoi, Vietnam (Ethical permission number IACUC-1603/22 issued on March 16, 2022).

In Vivo Experiment

Fifty Wistar rats were randomly allocated into five groups (n = 10/group) for the experiment. The groups were designated as follows:

Group 1 (Control Group): Received a standard laboratory diet and distilled water.
Group 2 (Disease Model Group): Induced with type 2 diabetes (T2DM) and administered distilled water.
Group 3 (Positive Control Group): Induced with T2DM and received gliclazide at a dose of 20 mg/kg/day.
Group 4 (VLDE-Low Dose): Induced with T2DM and administered VLDE at a dose of 620 mg/kg/day.
Group 5 (VLDE-High Dose): Induced with T2DM and administered VLDE at a dose of 1240 mg/kg/day.

Type 2 diabetes was induced in Wistar rats using a combination of a high-fat diet (HFD) and low-dose streptozotocin (STZ) injection. The HFD was formulated to provide 30% of energy from fat and 70% from carbohydrates. It contained a mixture of cholesterol, coconut oil, fructose, lard, corn flour, brewer's yeast, and calcium carbonate (specific composition percentages can be provided if available). Rats were fed this diet for four consecutive weeks. Following the HFD feeding period, rats received an intraperitoneal injection of STZ at a dose of 35 mg/kg body weight. The STZ was dissolved in 0.1 M citrate buffer at pH 4.5 to ensure optimal effectiveness. Blood glucose levels were measured 72 hours after STZ injection. Rats with blood glucose levels exceeding 200 mg/dL were classified as diabetic for the study. Subsequently, the diabetic rats continued on the HFD regimen, while all rats (diabetic and non-diabetic) received either distilled water or the assigned test drug according to their group allocation.

This treatment period lasted for 28 days. During the experiment, several parameters were assessed to evaluate the effects of the treatments:

Body weight: Body weight of each rat was measured at designated time points.
Food and water intake: Daily food and water consumption were monitored for each group.
Urine volume: Urine volume was measured to assess potential changes in fluid balance.
Blood glucose and insulin levels: Following an overnight fast, blood samples were collected from the retroorbital sinus (eye socket) for blood glucose and insulin level measurement. Insulin levels were determined using a commercially available ELISA kit (e.g., Rat Insulin ELISA Kit, Crystal Chem USA).

Insulin resistance indices

These indices were calculated using blood glucose and insulin data obtained at two specific time points:

T_0 (baseline): Immediately before drug administration.
T_c (treatment endpoint): One hour after the last drug administration on the final day.

The insulin resistance indices were calculated, including:

HOMA-IR (homeostatic model assessment of insulin resistance):
HOMA-IR = (blood glucose (mg/dL) × blood insulin (µIU/mL))/405
HOMA-β (homeostatic model assessment of pancreatic β-cell function):
HOMA-β = 20 × blood insulin (µIU/mL)/ (blood glucose (mMol/L) – 3.5)
QUICKI (quantitative insulin sensitivity check index):
QUICKI = 1/(log blood glucose (mg/dL) + log blood insulin(µIU/mL))
DI (insulin disposition index): DI = HOMA-β/HOMA-IR

Following blood collection for glucose and insulin analysis, the rats were euthanized humanely according to ethical guidelines. The pancreas was then swiftly dissected for histological examination. Pancreas weight, expressed as a percentage of body weight, was measured to assess potential changes in size. Harvested tissues were immediately fixed in a 10% formalin to preserve cellular morphology. Subsequently, histological slides were prepared and stained with hematoxylin and eosin (H&E) for routine tissue evaluation. The prepared slides were examined by qualified personnel at the Department of Pathological Anatomy, Hospital 103 (Hanoi, Vietnam), for any alterations in pancreatic tissue structure or cellular morphology. To assess the drug's efficacy, a comparative analysis of

blood glucose levels, insulin levels, and calculated insulin resistance indices was performed between groups..

Statistical Analysis

The results are presented as mean ± SD. Calculations were performed using Microsoft Excel software. Differences between groups were compared using One-way ANOVA (followed by LSD test), while differences between time points within the same group were compared using the Paired Samples T-test. Statistical significance was considered when $p < 0.05$.

Results and Discussion

Impact of VLDE on Rat Body Weight, Food Intake, and Water Consumption

Before drug administration (T_0), the type 2 diabetes-induced rats exhibited higher body weight, food intake, and water consumption compared to the control group, though these differences were not statistically significant ($p > 0.05$; Table 1). At the subsequent time point (T_c), one hour after administration of the final VLDE dose, the model group showed a decrease in body weight and an increase in water and food consumption relative to the control group ($p < 0.01$). These changes align with typical clinical manifestations of T2DM, confirming the successful induction of disease in the model group. In contrast, the groups receiving medication (groups 3, 4, 5) displayed increased body weight and decreased water and food consumption compared to the model group ($p < 0.05$), indicating a significant improvement in the pathological symptoms associated with type 2 diabetes.

Impact of VLDE on Blood Glucose and Insulin Levels in Rats

Before drug administration (T_0), the type 2 diabetes-induced groups (groups 2–5) had significantly higher blood glucose levels and lower blood insulin levels compared to the control group ($p < 0.01$; Table 2). Blood glucose levels in the type 2 diabetes-induced groups exceeded 200 mg/dL, confirming the presence of diabetes. One hour after administration of the final dose of VLDE (T_c), the model group exhibited a significant increase in blood glucose levels compared to T_0 ($p < 0.05$) and to the control group ($p < 0.01$). Conversely, blood insulin levels in the model group decreased significantly compared to both T_0 ($p < 0.05$) and the control group ($p < 0.01$). In groups being administered medication, or medication groups (groups 3–5), blood glucose levels were significantly lower at T_c than at T_0 ($p < 0.05$). Further, while their blood glucose levels were lower compared to the model group ($p < 0.05$), they remained higher than those in the control group across all medication groups ($p < 0.05$). Similarly, blood insulin levels in the medication groups (groups 3–5) at T_c increased significantly compared to T_0 ($p < 0.05$) and the model group ($p < 0.05$) but remained lower than in the control group ($p < 0.05$). These findings suggest that the research medication effectively reduces blood glucose levels and increases blood insulin levels in the diabetic rat model. Comparison between medication groups (groups 3–5) showed no significant differences in blood glucose and blood insulin levels ($p > 0.05$), indicating that VLDE at both dosage levels had effects comparable to those of gliclazide at 20 mg/kg/day.

Table 1. Evaluation of rat body weight, food intake, and water consumption.

Groups	Rat weigh (g)		Food intake (g/kg)		Water consumption (ml/kg)	
	T_o	T_c	T_o	T_c	T_o	T_c
Group 1 (1)	223.54 ± 15.01	253.68 ± 12.43	68.14 ± 8.96	94.25 ± 8.42	77.46 ± 9.28	96.27 ± 10.43
Group 2 (2)	231.22 ± 21.18	221.96$^{\Delta}$ ± 11.51	79.54 ± 9.42	186.37$^{\Delta}$ ± 21.42	82.96 ± 8.68	218.64$^{\Delta}$ ± 23.39
Group 3 (3)	229.88 ± 14.26	246.89* ± 11.52	73.65 ± 10.84	124.38* ± 16.53	86.91 ± 8.96	148.65* ± 16.28
Group 4 (4)	232.01 ± 13.60	245.24* ± 15.46	76.01 ± 8.86	133.12* ± 16.14	84.46 ± 9.53	159.08* ± 12.81
Group 5 (5)	233.71 ± 14.46	243.66* ± 15.39	77.09 ± 8.92	129.56* ± 18.65	81.13 ± 9.45	146.20* ± 13.65

Group 1 (control group): normal diet and distilled water; Group 2 (disease model group): induced type 2 diabetes (T2DM) + distilled water; Group 3 (positive control, gliclazide): induced T2DM + gliclazide at a dose of 20mg/kg/day; Group 4 (VLDE -dose 1): induced T2DM + VLDE at a dose of 620 mg/kg/day; Group 5 (VLDE -dose 2): induced T2DM + VLDE at a dose of 1240 mg/kg/day. *$^{\Delta}$ – $p < 0.01$ vs (1); * – $p < 0.05$ vs (2)* (n = 10 in each group, Mean ± SD).

Table 2. Impact of VLDE on blood glucose and insulin levels in rats.

Groups		Glucose level (mg/dL)			Insulin level (µIU/ml)		
		T_o	T_c	p_{c-o}	T_o	T_c	p_{c-o}
Group 1	(1)	93.51 ± 11.24	95.83 ± 12.01	> 0.05	35.94 ± 3.61	36.18 ± 3.42	> 0.05
Group 2	(2)	253.68$^{\Delta}$ ± 26.15	306.68$^{\Delta}$ ± 31.75	< 0.05	23.14$^{\Delta}$ ± 2.57	18.35$^{\Delta}$ ± 2.56	< 0.05
Group 3	(3)	249.92$^{\Delta}$ ± 24.61	145.96*$^{\blacktriangle}$ ± 16.62	< 0.05	22.96$^{\Delta}$ ± 2.43	28.93*$^{\blacktriangle}$ ± 2.38	< 0 05
Group 4	(4)	252.02$^{\Delta}$ ± 22.41	147.57*$^{\blacktriangle}$ ± 15.72	< 0.05	22.84$^{\Delta}$ ± 2.89	28.16*$^{\blacktriangle}$ ± 2.52	< 0.05
Group 5	(5)	249.09$^{\Delta}$ ± 19.39	142.67*$^{\blacktriangle}$ ± 13.25	< 0.05	23.03$^{\Delta}$ ± 3.02	29.15*$^{\blacktriangle}$ ± 2.63	< 0.05

*$^{\Delta}$ – $p < 0.01$ vs (1); $^{\blacktriangle}$ – $p < 0.05$ vs (1); * – $p < 0.05$ vs (2)*

Impact of VLDE on Some Insulin Resistance Indices

In the model group, the homeostatic model of insulin resistance (HOMA-IR) index was significantly higher compared to both the control group and the medication groups ($p < 0.05$). The HOMA of β-cell function (HOMA-β) and disposition index (DI) were significantly lower in the model group than in the control group and the medication groups ($p < 0.001$). Additionally, the quantitative insulin sensitivity check index (QUICKI) was significantly lower compared to both the control group and the medication groups ($p < 0.05$; Table 3). In the medication groups (groups 3–5), the HOMA-IR and QUICKI indices were restored to levels comparable to the control group ($p > 0.05$) and were significantly different from the model group ($p < 0.05$). The HOMA-β and DI indices in the medication groups were significantly increased compared to the model group ($p < 0.001$), although they remained significantly different from the control group ($p < 0.05$). Comparative analysis of the medication groups (groups 3–5) revealed

no significant differences in insulin resistance indices among the groups ($p > 0.05$). These findings indicate that VLDE at both administered doses exerts effects on insulin resistance indices comparable to gliclazide at 20 mg/kg/day.

Changes in Pancreas Weight Percentage Relative to Body Weight

Rats in the model group (group 2) displayed a significantly lower percentage of pancreas weight relative to body weight compared to the group (group 1; $p < 0.01$). Groups of rats treated with gliclazide at 20 mg/kg/day (group 3) and groups treated with both dose 1 (group 4) and dose 2 (group 5) of VLDE had a significantly higher pancreas-to-body weight ratio compared to the model group ($p < 0.01$). Compared to the controls, rats treated with gliclazide at 20 mg/kg/day (group 3) and VLDE at both doses (groups 4 and 5) exhibited a lower percentage of pancreas weight relative to body weight, though this difference was not statistically significant ($p > 0.05$). These results suggest that gliclazide at 20 mg/kg/day and VLDE at both doses increase the pancreas-to-body weight ratio in type 2 diabetic rats to levels comparable to the control group ($p > 0.05$). No significant differences were observed among the pancreas-to-body weight ratios among the treatment groups ($p > 0.05$).

Table 3. Impact of VLDE on some insulin resistance evaluation indices.

Groups		HOMA-IR	HOMA-β	QUICKI	DI
Group 1	(1)	4.39 ± 0.51	110. 73 ± 15.85	0.309 ± 0.006	25.28 ± 3.94
Group 2	(2)	6.32 ± 0.88	37. 79 ± 5.23	0.292 ± 0.005	5.98 ± 0.86
Group 3	(3)	4.45 ± 0.67	76. 97 ± 10.43	0.302 ± 0.006	17.36 ± 2.41
Group 4	(4)	4.42 ± 0.58	74. 56 ± 9.32	0.305 ± 0.004	16.65 ± 2.12
Group 5	(5)	4.36 ± 0.54	79. 05 ± 9.91	0.307 ± 0.007	18.03 ± 2.38
		$p_{2-1} < 0.05$	$p_{2-1} < 0.001$	$p_{2-1} < 0.05$;	$p_{2-1} < 0.001$;
		$p_{3.4.5-2} < 0.05$;	$p_{3.4.5-2} < 0.001$;	$p_{3.4.5-2} < 0.05$;	$p_{3.4.5-2} < 0.001$;
p		$p_{3.4.5-1} > 0.05$;	$p_{3.4.5-1} < 0.01$;	$p_{3.4.5-1} > 0.05$;	$p_{3.4.5-1} < 0.01$;
		$p_{4.5-3} > 0.05$;	$p_{4.5-3} > 0.05$;	$p_{4.5-3} > 0.05$;	$p_{4.5-3} > 0.05$;
		$p_{4-5} > 0.05$	$p_{4-5} > 0.05$	$p_{4-5} > 0.05$	$p_{4-5} > 0.05$

Table 4. Percentage of pancreas weight relative to body weight.

Groups		Percentage of pancreas weight (%)	% decrease vs (1)	% increase vs (2)
Group 1	(1)	0.943 ± 0.058	-	-
Group 2	(2)	0.521 ± 0.036	44.77	-
Group 3	(3)	0.912 ± 0.065	3.30	75.08
Group 4	(4)	0.894 ± 0.069	5.21	71.63
Group 5	(5)	0.920 ± 0.066	2.47	76.59

$p_{-2} < 0.01$; $p_{3,4-1} > 0.05$; $p_{4-3} > 0.05$; (-) not determine.

Histopathological Images of the Pancreas

Histopathological images of the pancreas serve to illustrate alterations in pancreatic morphology, including changes in size, cellular structure, and tissue organization relative to normal physiological conditions. In our study, the histological examination reveals distinct lobules within the pancreatic tissue, separated by thin fibrous septa (Figure 1). The exocrine glands display abundant pink secretory material (Figure 1a), while the islets of Langerhans exhibit cells with a distinctly bright appearance (Figure 1b). In the model group, the islets of Langerhans are notably smaller compared to both the control and the drug-treated groups (Figure 1c). Conversely, in the drug-treated groups, there is a notable restoration of the size of the islets of Langerhans approaching levels comparable to those observed in the control group (Figure 1d,e). T2DM is characterized by insulin resistance and impaired insulin secretion from pancreatic β-cells.[18] The type 2 diabetes model in white rats, induced by a high-fat diet combined with low-dose streptozotocin, replicates both features of the disease and mirrors the mechanisms and characteristics of human T2DM.[19,20] Gliclazide, administered at a dose of 20 mg/kg/day, was selected as the reference drug for comparison due to its clinical efficacy in managing T2DM. The study results demonstrated clear manifestation of type 2 diabetes in the model group, including increased blood glucose levels, decreased insulin levels, significant changes in peripheral insulin resistance indices, increased food and water intake, weight loss, and minor damage to pancreatic tissue, particularly the islets of Langerhans. Moreover, the experimental model demonstrated the ability of VLDE to improve clinical symptoms of type 2 diabetes, comparable to the reference drug gliclazide.

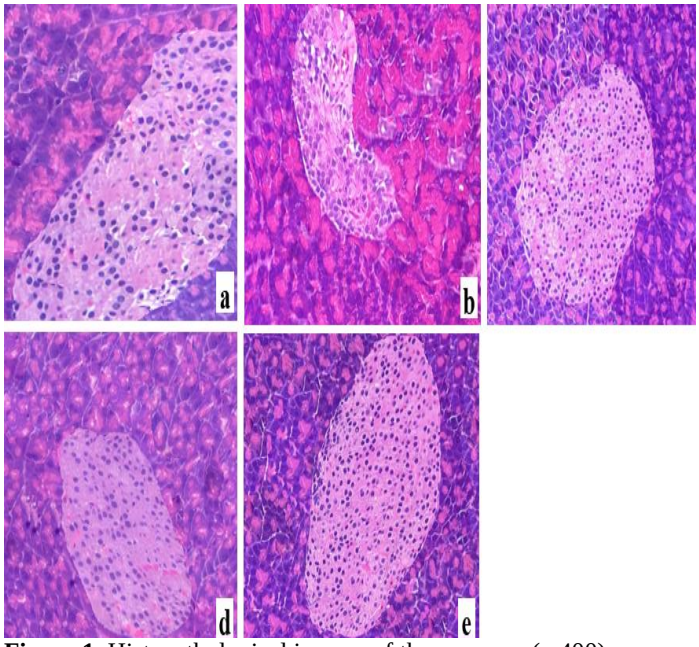

Figure 1. Histopathological images of the pancreas (x 400).
(a): normal diet and distilled water; (b): induced type 2 diabetes (T2DM) + distilled water; (c): induced T2DM + gliclazide at a dose of 20mg/kg/day; (d) induced T2DM + VLDE at a dose of 620 mg/kg/day; and (e): induced T2DM + VLDE at a dose of 1240 mg/kg/day.

The study results align with previous publications examining the effects of *L. speciosa* in lowering blood glucose, particularly due to compounds such as corosolic acid, which reduces blood sugar by increasing insulin sensitivity, enhancing glucose absorption, and inhibiting α-glucosidase.[8,9] In addition to corosolic acid, ellagitannin compounds—specifically lagerstroemin, flosin B, and reginin A—have been shown to regulate blood glucose levels. These compounds promote glucose uptake by activating glucose transporter type 4 (GLUT4), a protein responsible for transporting glucose from the blood into muscle cells and adipocytes.[9] In this study, modern extraction processes have been successfully utilized to isolate active ingredients from medicinal herbs, which have subsequently demonstrated efficacy in lowering blood glucose levels. These results lay a strong foundation for exploring the use of dried extracts from banaba leaves (*L. speciosa*) in the prevention and treatment of T2DM, warranting further pre-clinical and clinical research.

Conclusion

In conclusion, administration of leaf extract from *L. speciosa* harvested in Vietnam at doses of 620 mg/kg/day and 1240 mg/kg/day for 28 days demonstrates efficacy in lowering blood glucose levels in rats induced with type 2 diabetes through a high-fat diet and low-dose streptozotocin. Both doses effectively lower blood glucose levels, increase insulin levels, restore pancreatic *β*-cell function, and improve insulin sensitivity, as evidenced by reductions in HOMA-IR and increases in HOMA-*β*, QUICKI, and DI indices. Furthermore, they increase the percentage of pancreatic weight relative to body weight and alleviate symptoms such as increased food and water intake and weight loss. Notably, over 28 days of treatment administration, the 1240 mg/kg/day dose exhibits greater efficacy in treating type 2 diabetes compared to the 620 mg/kg/day dose. These results suggest the potential utility of *L. speciosa* leaf extract in the prevention and treatment of T2DM.

Conflicts of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgment

The author team would like to express sincere gratitude to the Department of Pharmacology at the Vietnam Military Medical University, Vietnam for providing the facilities to conduct this research.

References

1. Roden M, Shulman GI. The integrative biology of type 2 diabetes. Nature. 2019;576(7785): 51-60.
2. International Diabetes Federation. IDF Diabetes Atlas. International Diabetes Federation; 2015.
3. The growing burden of diabetes in Viet Nam. Accessed July 25, 2022. https://www.who.int/vietnam/news/feature-stories/detail/the-growing-burden-of-diabetes-in-viet-nam
4. Hippisley-Cox J, Coupland C. Diabetes treatments and risk of amputation, blindness, severe kidney failure, hyperglycaemia, and hypoglycaemia: open cohort study in primary care. BMJ. 2016; 352:i1450.
5. Marshall SM, Flyvbjerg A. Prevention and early detection of vascular complications of diabetes. BMJ. 2006; 333(7566):475-480.
6. Blahova J, Martiniakova M, Babikova M, Kovacova V, Mondockova V, Omelka R. Pharmaceutical drugs and natural therapeutic products for the treatment of type 2 diabetes mellitus. *Pharmaceuticals.* 2021; *14*(8):806.
7. Chan EWC, Wong SK, Chan HT. An overview of the phenolic constituents and pharmacological properties of extracts and compounds from *Lagerstroemia speciosa* leaves. Trop J Nat Prod Res. 2022; 6(4):470-479.
8. Cannarella R, Vincenzo G, Aldo EC. Anti-dyslipidemic and anti-diabetic properties of corosolic acid: a narrative review. Endocrines. 2023; 4(3):616-629.
9. Miura T, Takagi S, Ishida T. Management of diabetes and its complications with Banaba (*Lagerstroemia speciosa* L.) and corosolic acid. Evid Based Complementt Alternat Med. 2012; 2012:871495.
10. Mousa AM, El-Sammad NM, Abdel-Halim AH, Anwar N, Khalil WKB, Nawwar M, Hashim AN, Elsayed EA, Hassan SK. *Lagerstroemia speciosa* (L.) Pers leaf extract attenuates lung tumorigenesis via alleviating oxidative stress, inflammation and apoptosis. Biomolecules. 2019; 9(12):871.
11. Singh TR, Ezhilarasan D. *Lagerstroemia speciosa* (L.) Pers., ethanolic extract attenuates simultaneously administered isoniazid- and dapsone-induced hepatotoxicity in rats. J Food Biochem. 2021; 45:e13830.
12. Sinelius S, Lady J, Yunardy M, Tjoa E, Nurcahyanti ADR. Antibacterial activity of *Lagerstreomia speciosa* and its active compound, corosolic acid, enhances cefotaxime inhibitory activity against *Staphylococcus aureus*. J Appl Microbiol. 2023; 134(8):lxad171.
13. Kawade A, Yamamura A, Kondo R, Suzuki Y, Yamamura H. Corosolic acid ameliorates vascular remodeling in pulmonary arterial hypertension via the downregulation of STAT3 signaling. J Pharmacol Sci. 2023; 151(2):119-127.
14. Saumya SM, Basha PM. Antioxidant effect of *Lagerstroemia speciosa* Pers (Banaba) leaf extract in streptozotocin-induced diabetic mice. Indian J Exp Biol. 2011; 49(2):125-131.
15. Shashiraj KN, Hugar A, Kumar RS, Rudrappa M, Bhat MP, Almansour AI, Perumal K, Nayaka S. Exploring the antimicrobial, anticancer, and apoptosis inducing ability of biofabricated silver nanoparticles using *Lagerstroemia speciosa* flower buds against the human osteosarcoma (MG-63) cell line via flow cytometry. Bioengineering (Basel). 2023; 10(7):821.

16. Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. J Basic Clin Pharm. 2016; 7(2):27-31.
17. Nair A, Morsy MA, Jacob S. Dose translation between laboratory animals and human in preclinical and clinical phases of drug development. Drug Dev Res. 2018; 79(8):373-382.
18. American Diabetes Association. Standards of Medical Care in Diabetes-2017 Abridged for Primary Care Providers. Clinical diabetes: a publication of the American Diabetes Association. 2017; 35(1):5-26.
19. Basatinya AM, Sajedianfard J, Nazifi S, Hosseinzadeh S. The analgesic effects of insulin and its disorders in streptozotocin-induced short-term diabetes. Physiol Rep. 2024; 12(8):e16009.
20. Lelyte I, Ahmed Z, Kaja S, Kalesnykas G. Structure-function relationships in the rodent streptozotocin-induced model for diabetic retinopathy: A systematic review. J Ocul Pharmacol Ther. 2022; 38(4):271-286.