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Original Research Article

Antidiabetic potential of seven-herb Thai formula: Effect on blood glucose, lipid profile, and pancreatic islet restoration in diabetic rats

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Abstract

Purpose: *To assess an aqueous extract from a traditional Thai herbal formula for hypoglycemic activity in streptozotocin-induced diabetic rats.*
Methods: *The rats were divided into six groups, each consisting of 8 animals as follows: normal and diabetic controls, received distilled water (1 mL/kg); a glibenclamide-treated positive control (5 mg/kg); and three groups received orally the herbal extract at doses of 125, 250 or 500 mg/kg body weight. Treatment was for a duration of four weeks, once daily. Changes in body weight, fasting blood glucose levels, hemoglobin (HbA1c) levels, liver and kidney function results before and after the administration of the extracts were observed. Histological examination of the pancreatic cells was also conducted.*
Results: *Administration of 250 mg/kg of these herbal formula extracts to diabetic rats resulted in a significant reduction in HbA1c levels, a notable decrease in fasting blood glucose, and a significant increase ($p < 0.05$) in body weight relative to diabetic controls. Organ weights and other hematological values remained unchanged. Significant reductions ($p < 0.05$) in triglycerides, total cholesterol, and AST/ALT levels were seen, compared to diabetic controls. Histological analysis showed that the treatment dose-dependently restored pancreatic islet architecture, especially at 250 mg/kg, suggesting tissue regeneration.*
Conclusion: *These promising results support the need for further studies to identify the active compounds and understand the mechanism of action.*

Keywords: *Thai herbal medicine, Diabetes mellitus, Hypoglycemic, Streptozotocin-induced diabetes, Pancreatic cells, Hemoglobin, Glibenclamide*

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INTRODUCTION

Diabetes mellitus represents a substantial global health challenge, with its incidence escalating worldwide, accentuating an urgent need for effective management strategies [1]. While modern pharmaceuticals have significantly advanced diabetes treatment, there remains a

compelling interest in traditional herbal remedies, especially in regions with a rich ethnobotanical heritage such as Thailand [2]. Thai traditional medicine, known for its holistic approach to health and well-being, provides a distinctive perspective on diabetes treatment through its use of complex herbal formulations [3]. One notable formulation from Thai folk medicine includes a combination of seven herbs: *Clerodendrum paniculatum* pagoda flower, (Lamiaceae), *Arcangelisia flava*, yellow fruit moonseed (Menispermaceae), *Suregada multiflora* (Euphorbiaceae), *Dendrophthoe pentandra*, a mistletoe species (Loranthaceae), *Tectona grandis*, teak (Lamiaceae), *Derris scandens*, and *Salacia chinensis* (Leguminosae). This formulation is not only a testament to the sophisticated understanding of plant synergies in traditional Thai medicine but also reflects a deep integration of cultural knowledge into medical practice [4].

Studies on these individual herbs have revealed significant anti-diabetic properties. *Clerodendrum paniculatum* has shown a hypoglycemic effect *in vitro, in vivo* and *ex vivo* models [5]. *Arcangelisia flava* contains berberine, a compound noted for its efficacy in lowering glucose levels [6]. *Suregada multiflora* is recognized for its antioxidant properties, which play a crucial role in managing diabetic complications [7]. *Dendrophthoe pentandra* has demonstrated antihyperglycemic effects [8], while *Tectona grandis* has been associated with the regulation of glucose metabolism [9]. *Derris scandens* has been found to improve insulin sensitivity [10], and *Salacia chinensis* is well-known for its anti-diabetic properties, particularly its ability to inhibit alpha-glucosidase, a key enzyme in carbohydrate digestion [11].

The integration of multiple herbs into a single formulation is a hallmark of Thai traditional medicine, which strategically employs complex herbal mixtures to address multifaceted health issues such as diabetes [12]. This practice is predicated on the belief that combining different herbs leads to synergistic effects, thereby offering a more comprehensive treatment approach by simultaneously targeting various aspects of the disease [13]. Recent scientific endeavors have increasingly focused on validating these traditional herbal formulations through rigorous research methodologies. Empirical studies have demonstrated that similar multi-herb combinations effectively control blood glucose levels, enhance insulin sensitivity, and manage diabetic complications [14]. Nonetheless, it is crucial to acknowledge that, although the individual components of this specific formulation have been studied, knowledge of their combined effects remains relatively sparse.

The burgeoning interest in traditional herbal medicine accentuates a broader trend of integrating age-old knowledge with contemporary scientific methodologies in diabetes management [15]. This approach seeks to harness the therapeutic potential of herbal remedies, ensuring their safety and efficacy through rigorous, evidence-based practices. Not only does this strategy honor cultural heritage, but it also enriches the array of options available for diabetes treatment, potentially paving the way for more personalized and effective therapeutic interventions. Thus, the present study aims to contribute to the field by investigating the hypoglycemic activity of an aqueous extract from a traditional Thai herbal formula and its effects on streptozotocin-induced diabetic rats.

EXPERIMENTAL

Plant material collection

The seven medicinal plants were harvested from local cultivation areas in Maha Sarakham Province, Northeastern Thailand, from May - June 2020. Assistant Professor Piyaphong Yupparach authenticated the specimens, which were deposited at the Faculty of Medicine, Mahasarakham University, Thailand. Each plant was assigned a unique code: *C. paniculatum* (MSU.MED-CP0001/AK), *A. flava* (MSU.MED AF0001/AK), *S. multiflora* (MSU.MED SM0001/AK), *D. pentandra* (MSU.MED-DP0001/AK), *T. grandis* (MSU.MED-TG0001/AK), *D. scandens* (MSU.MED-DS0001/AK), and *S. chinensis* (MSU.MED-SC0001/AK). The fresh plant materials of *C. paniculatum* root, *A. flava* stem, *S. multiflora* wood, *D. pentandra* whole, *T. grandis* leaf, *D. scandens* stem and *S. chinensis* stem were thoroughly cleaned and then dried in a hot air oven at 60 °C for 24 hours before being ground into a fine powder.

Preparation of aqueous extract from a traditional Thai herbal recipe

The preparation of the aqueous extract involved a traditional Thai herbal recipe, consisting of equal proportions of *C. paniculatum*, *A. flava, S. multiflora, D. pentandra*, *T. grandis*, *D. scandens* and *S. chinensis* (1:1:1:1:1:1:1 w/w). The extraction method entailed boiling the powdered herbs in distilled water at 1 g: 1,000 mL for 15 minutes, a process repeated twice to enhance the yield of water-soluble phytochemicals.

Following boiling, the mixture was filtered using Whatman® filter papers (Germany) to remove any solid residues. The filtrate was then concentrated at 85 °C using a Buchi Rotavapor® R-300 (Switzerland) and subsequently freeze-dried to produce a dark brown powder. This powder was stored under refrigeration at temperatures below 4 °C to preserve its bioactive compounds for future in vivo studies. This thorough extraction process is designed to optimize the recovery of active ingredients while maintaining the potential synergistic effects inherent in the traditional formulation, ensuring the integrity and efficacy of the extract for medicinal use.

Animals

Male albino Wistar rats weighing between 180 - 200 g were procured from the North-Eastern Laboratory Animal Centre (NELAC) at Khon Kaen University, Thailand. These rats were acclimatized over five days in an air-conditioned facility maintained at 23 °C, with a 12-hour light/dark cycle and relative humidity kept between 30 - 60 %. Throughout this period, the rats had unrestricted access to standard chow and water. Following acclimatization, the procedures commenced, adhering strictly to the ethical guidelines set by the Committee Care and Use of Laboratory Animal Resources of the National Research Council of Thailand. The protocol was approved by the Institutional Animal Care and Use Committee of Khon Kaen University (approval no. IACUC-KKU-67/2020). All animal care and procedures were followed in compliance with established ethical standards.

Determination of hypoglycemic activity

Male rats were stratified into six groups (n = 8 per group) to evaluate the hypoglycemic effects of a traditional herbal extract compared to controls and a standard antidiabetic drug. The groups were organized as follows: Group I (Normal control) and Group II (Diabetic control) both received distilled water (1 ml/kg); Group III (Positive control) comprised diabetic rats treated with 50 mg/kg body weight of glibenclamide; Groups IV to VI consisted of diabetic rats treated with the herbal extract at dosages of 125, 250, and 500 mg/kg, respectively. All treatments, including the herbal extract and glibenclamide, were suspended in distilled water and administered orally at 1 mL per animal using an orogastric tube once daily for four weeks. This experimental design was implemented to assess the efficacy of multiple dosages of the herbal extract in modulating blood glucose levels relative to both baseline diabetic conditions and the effects of glibenclamide, facilitating a comprehensive analysis of its therapeutic potential.

Induction of diabetes in rats

Diabetes was induced in rats through a single intraperitoneal injection of streptozotocin (STZ, Sigma Chemicals, St. Louis, MO) at a dose of 65 mg/kg body weight, with STZ freshly dissolved in a cold 20 mM citrate buffer (pH 4.5) [16]. To alleviate potential hypoglycemia-induced discomfort following the injection, rats were provided with a 2 % sucrose solution for 48 hours. Three days post-STZ administration, fasting blood glucose (FBG) levels were measured. Rats displaying FBG levels exceeding 126 mg/dL were classified as diabetic and subsequently included in the study [17]. This induction method has been optimized to ensure a consistent and reliable diabetic model, which is crucial for the evaluation of the hypoglycemic effects of the herbal extract being studied.

Determination of fasting blood glucose (FBG)

Fasting blood glucose (FBG) levels were systematically measured in both normal and streptozotocin (STZ)-induced diabetic rats over four weeks to monitor the progression and control of diabetes. Blood samples were collected from the tail veins of rats after an overnight fast. FBG readings were taken at baseline and subsequently at the end of each week (weeks 1, 2, 3, and 4) using an Accu-check Guide glucometer (Roche, Germany). This consistent monitoring strategy is crucial for evaluating the dynamic changes in glucose levels due to induced diabetes and any potential interventions, providing a detailed temporal profile of the metabolic impact of the diabetes induction and subsequent treatments.

Determination of hematological and clinical chemistry parameters

Following the completion of the 4 weeks of therapy, the rats were subjected to an overnight fast and then euthanized by intraperitoneal injection of thiopental sodium at a dose of 85 mg/ml/kg [18]. The blood samples were extracted from the cardiac tissue of the rat. The hematological parameters, such as red blood cells (RBC), hemoglobin (Hb), hematocrit (Hct), platelet count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cells (WBC), lymphocytes, monocytes, and neutrophils, were measured using an automated blood analyzer (Sysmex XS

800i, Japan). The clinical chemistry parameters, such as blood urea nitrogen (BUN), creatinine, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), and hemoglobin A1c (HbA1C) were assessed using an automated blood chemical analyzer (Cobas Integra 400 plus, Germany), located in the Community Clinical Laboratory Faculty of Associated Medical Science at Khon Kaen University in Thailand.

Pancreatic tissue sampling for histopathological examination

At the end of the period, the last blood sample was collected. Histopathological study of the pancreas tissues was done by first preserving the tissues in 10 % neutral formalin for histological analysis. Afterward, the tissues were rinsed with normal saline and immediately placed in 10 % formalin for 72 hours, with the fixative solution being changed daily. The tissues were then desiccated using a sequence of alcohols and xylene in the tissue processing equipment. The desiccated tissues were sliced into minute fragments and placed in cassettes. The tissues were immersed in paraffin and sliced into sections with a thickness of 5 - 7 µm using a rotary microtome. The tissue samples coated with ribbon-like paraffin were immersed in a warm water bath to eliminate the paraffin. The tissues were affixed to a microscope slide and subjected to staining with hematoxylin and eosin. The histopathology micrographs were obtained using an Olympus BX51TF light microscope (Olympus Inc., Japan) and a digital camera EP50 (Olympus Inc., Germany) [19].

Statistical analysis

Statistical analyses of the data were performed using one-way analysis of variance (ANOVA), followed by Duncan's multiple range tests to identify significant differences among the groups. Data are presented as mean ± standard error of the mean (SEM). A *p*-value of less than 0.05 was established as the threshold for statistical significance, ensuring that findings deemed significant were unlikely to be due to random variation. This robust statistical method allows for precise comparisons between groups, validating the results and their implications for the hypotheses.

RESULTS

Effect of the aqueous extract on body weight

Table 1 illustrates the impact of a Thai herbal extract on body weight changes in streptozotocin (STZ)-induced diabetic rats over four weeks. The diabetic control (DM-Control) group showed a slight weight decrease of 1.31%. Diabetic rats treated with glibenclamide and the herbal extract demonstrated significant weight gains: 42.74 % in the DM-GB group (treated with glibenclamide), 38.95 % in the DM-125 group (125 mg/kg dosage), 49.55 % in the DM-250 group (250 mg/kg dosage), and 34.62 % in the DM-500 group (500 mg/kg dosage), all with statistical significance ($p < 0.05$). Specifically, the DM-250 group showed the highest increase in weight, while the DM-500 group, despite receiving the highest dose, exhibited a comparatively lower weight gain than the groups receiving lower doses. These findings suggest that the herbal extract may play a beneficial role in weight management for diabetic rats, with varying efficacy across different doses.

Effect of aqueous extract on fasting blood glucose (FBG) and hemoglobin A1c (HbA1C)

Table 2 highlights the significant impact ($p < 0.05$) of an aqueous Thai herbal extract on fasting plasma glucose levels in streptozotocin-induced diabetic rats, as measured over four weeks.
Among the various doses tested, the 250 mg/kg dosage (DM-250) proved to be the most effective, reducing fasting plasma glucose levels by 30.52 %. The hypoglycemic effect was more pronounced at the mid and high doses, particularly at 250 and 500 mg/kg. Conversely, the treated groups exhibited notable significant reductions ($p < 0.05$) in HbA1c levels compared to the diabetic control (DM-Control) group, indicating improved long-term glucose regulation. The glucose-lowering effect of the extract was found to be consistent throughout the

experiment, with the rats maintaining stable glucose levels throughout the four weeks. This evidence supports the potential of the herbal extract as an effective intervention for managing hyperglycemia in diabetic conditions.

Relative organ weight

Table 3 presents data on the relative organ weights (expressed as percentages) of the liver, kidney, heart, spleen, lung, and pancreas among various treatment groups, including the non-diabetic control (NM-Control), diabetic control

(DM-Control), and diabetic groups treated with different doses of the herbal extract (DM-GB, DM-125, DM-250, DM-500). The analysis revealed no statistically significant differences in the organ weights across these groups. This finding indicates that the herbal extract, administered in varying doses, did not adversely affect the organ weights of treated rats, suggesting its safety in terms of organ health and mass maintenance across the tested doses.

Hematological values

Table 4 presents the effects of glibenclamide and an aqueous extract derived from a traditional Thai herbal recipe on various hematological markers in streptozotocin (STZ)-induced diabetic rats. The results indicate that there were no statistically significant differences in red blood cell (RBC) count, hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and white blood cell (WBC) counts across the different treatment groups. This includes the normal control (NM-Control), the diabetic control (DM-Control), and diabetic rats treated with various doses of the herbal extract.
However, a noteworthy observation was made regarding platelet counts, which were significantly higher *($p < 0.05$)* in the NM-Control group (1118.40 x 10^3/µL) compared to the diabetic groups, both untreated and treated with the herbal extract. This suggests that while the herbal extract did not adversely affect most blood cell parameters, it did influence platelet counts as seen by a significant reduction ($p < 0.05$) overall indicating its neutrality in impacting hematological values in diabetic rats.

Clinical chemistry values

Table 5 reveals that an aqueous extract derived from a traditional Thai herbal recipe significantly improved several biochemical parameters in streptozotocin (STZ)-induced diabetic rats, indicating a positive impact on metabolic health ($p < 0.05$). Specifically, diabetic rats treated with the extract exhibited significantly lower levels ($p < 0.05$) of blood urea nitrogen (BUN), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) compared to those in the diabetic control (DM-Control) group, suggesting enhanced renal and hepatic function. In addition, significant decreases ($p < 0.05$) in alkaline phosphatase (ALP), triglycerides (TG), and total cholesterol (TC) levels were observed, which indicates improved lipid metabolism. Specifically, the DM-125 and DM-250 treatment groups showed the most significant improvements across these parameters. Furthermore, creatinine levels remained consistent across all groups, highlighting the extract's safety regarding kidney function. Interestingly, high-density lipoprotein (HDL) levels in diabetic rats were higher compared to the non-diabetic control (NM-Control) group, and there were no significant differences among the treatment groups in terms of HDL levels. Jointly, these findings disclose that the herbal extract effectively ameliorates various metabolic disturbances associated with diabetes.

Histological characteristics of the pancreas

Figure 1 presents the histological characteristics of the pancreas in both normal rats and streptozotocin (STZ)-induced diabetic rats, detailing changes in the Islets of Langerhans. In the NM-Control group, the pancreatic islets maintain an undamaged architecture, exhibiting robust structural integrity. Conversely, the DM-Control group shows islets that are significantly smaller and oval, highlighting the deleterious effects of diabetes on pancreatic morphology. The DM-GB treatment group exhibits partial improvement in islet structure, suggesting some therapeutic efficacy. Further, the treatment groups DM-125, DM-250, and DM-500 display improvements that vary with dosage; particularly, the DM-500 group shows the most significant restoration in terms of both size and cellular organization of the islets. Higher magnification views (×20) reveal more detailed cellular features, confirming these observations across all groups and stressing the potential of varying doses of the treatment to differentially influence pancreatic histology in diabetic conditions.

Table 1: Effect of a Thai herbal extract and glibenclamide on Body Weight in diabetic rats compared to normal and diabetic control rats

Group	Day 1 (g)	Week 1 (g)	Week 2 (g)	Week 3 (g)	Week 4 (g)	Body weight gain (%)
NM-Control	211.62±11.83^{Aa}	305.51±14.09^{Cb}	321.60±15.09^{Cc}	349.98±18.08^{Dd}	366.66±20.37^{De}	73.26
DM-Control	206.39±7.23^{Aa}	203.09±3.61^{Aa}	210.54±6.98^{Aa}	210.36±6.53^{Aa}	203.69±6.08^{Aa}	−1.31
DM-GB	203.09±3.61^{Aa}	215.93±14.90^{Aa}	241.52±18.86^{Bb}	252.79±23.36^{Bb}	289.89±27.56^{Bc}	42.74
DM-125	210.54±6.98^{Aa}	237.68±11.48^{Bb}	254.21±14.51^{Bb}	260.72±19.75^{Bb}	292.55±18.38^{Bc}	38.95
DM-250	210.36±6.53^{Aa}	234.69±13.84^{Bb}	265.46±15.34^{Bb}	293.41±21.19^{Cc}	314.60±21.29^{Cc}	49.55
DM-500	203.69±6.75^{Aa}	234.12±15.79^{Bb}	223.95±17.58^{Bb}	247.81±14.83^{Bb}	274.20±14.22^{Bc}	34.62

Different letters (A, B, C, D) in each column indicated significant differences at $p < 0.05$, Different letters (a, b, c, d) in each row indicated significant differences at $p < 0.05$. Values are presented as mean ± SEM, n = 8 per group

Table 2: The fasting blood glucose levels (FBG) and hemoglobin A1c (HbA1C) of diabetic rats treated with glibenclamide and Thai herbal aqueous extract at different doses

Group	Fasting Plasma glucose concentrations (mg/dL)					FBG (%)	HbA1C (%)
	Day 1	Week 1	Week 2	Week 3	Week 4		
NM-Control	104.15±1.72^{Aa}	101.47±1.41^{Aa}	105.43±1.47^{Aa}	105.63±0.89^{Aa}	105.00±1.41^{Aa}	0.81	5.9±0.20^{A}
DM-Control	502.80±27.03^{Ca}	501.52±21.70^{Da}	527.25±11.03^{Db}	580.75±23.03^{Bb}	587.50±12.18^{Cb}	14.42	13.0±0.22^{B}
DM GB	490.78±29.16^{Cc}	245.75±57.29^{Ca}	387.75±22.42^{Cb}	475.38±23.12^{Dc}	549.00±31.30^{Cd}	10.60	12.8±0.44^{B}
DM-125	411.48±33.26^{Bb}	223.13±31.86^{Ca}	194.45±22.73^{Ba}	358.24±46.75^{Cb}	558.88±28.64^{Cb}	26.37	12.8±0.8^{B}
DM-250	409.50±48.59^{Bb}	141.25±8.57^{Ba}	202.63±5.21^{Ba}	348.38±26.43^{Ca}	313.75±32.63^{Bb}	−30.52	11.1±1.79^{B}
DM-500	397.32±32.89^{Ba}	135.50±53.70^{Ba}	146.00±43.92^{Ba}	224.25±25.24^{Ba}	344.63±31.74^{Ba}	−15.29	12.1±1.00^{B}

Different letters (A, B, C, D) in each column indicated significant differences at $p < 0.05$. Different letters (a, b, c, d) in each row indicated significant differences at $p < 0.05$. Values are presented as mean ± SEM, n = 8 per group

Table 3: The relative organ weight of diabetic rats treated with glibenclamide and the Thai herbal aqueous extract at different doses

Group	Relative organ weight (%), mean ± SEM					
	Liver	Kidney	Heart	Spleen	Lung	Pancreatic
NM-Control	15.28±2.00^{a}	2.03±0.25^{a}	1.63±0.35^{a}	1.06±0.13^{a}	2.06±0.35^{a}	1.51±0.39^{a}
DM-Control	14.90±2.66^{a}	1.77±0.28^{a}	1.23±0.23^{a}	0.85±0.38^{a}	1.61±0.22^{a}	1.20±0.11^{a}
DM-GB	12.96±1.74^{a}	1.61±0.21^{a}	1.28±0.16^{a}	0.71±0.19^{a}	1.54±0.14^{a}	1.18±0.35^{a}
DM-125	12.23±0.94^{a}	1.59±0.18^{a}	1.27±0.15^{a}	0.75±0.12^{a}	1.52±0.11^{a}	1.14±0.33^{a}
DM-250	14.98±1.67^{a}	1.88±0.16^{a}	1.36±0.25^{a}	0.92±0.24^{a}	1.69±0.16^{a}	1.04±0.20^{a}
DM-500	13.20±2.17^{a}	1.78±0.26^{a}	1.25±0.18^{a}	0.77±0.24^{a}	1.51±0.22^{a}	1.14±0.45^{a}

Mean values followed by distinct uppercase letters (a, b, c, d) within the same columns indicate statistically significant differences ($p < 0.05$; n = 8)

Table 4: Hematological parameters of diabetic rats treated with glibenclamide and different doses of a Thai herbal extract

Group	Hematological parameters in normal and STZ-induced diabetic rats (Mean ± SEM)							
	RBC (10^3/µL)	***Hb (g/dL)***	***Hct (%)***	***MCV (fL)***	***MCH (pg)***	***MCHC (g/dL)***	***PLT (10^3/µL)***	***WBC (10^3/µL)***
NM-Control	7.72±0.36[a]	13.86±0.84[a]	42.00±2.83[a]	54.36±3.96[a]	18.00±1.04[a]	33.10±0.78[a]	1118.40±50.89[b]	6.40±1.34[a]
DM-Control	8.52±1.03[a]	15.56±1.62[a]	50.40±6.50[a]	59.54±3.21[a]	18.30±0.45[a]	30.76±1.35[a]	952.60±273.65[a]	6.03±2.27[a]
DM-GB	8.54±0.64[a]	14.82±0.68[a]	47.83±2.56[a]	56.12±4.46[a]	17.40±1.09[a]	31.05±0.70[a]	830.17±131.93[a]	4.15±1.50[a]
DM-125	8.56±0.52[a]	15.15±0.71[a]	47.50±2.17[a]	55.28±1.62[a]	17.72±0.50[a]	32.03±0.32[a]	793.67±101.49[a]	3.67±0.96[a]
DM-250	8.71±0.78[a]	15.50±1.00[a]	48.50±3.73[a]	55.78±1.97[a]	17.85±0.65[a]	32.02±0.83[a]	966.83±142.45[a]	5.73±1.88[a]
DM-500	7.86±1.43[a]	14.93±1.25[a]	46.57±8.12[a]	59.41±2.51[a]	19.46±3.03[a]	32.71±4.60[a]	825.43±108.15[a]	4.18±1.34[a]

The mean values followed by distinct uppercase letters (a) within the same columns indicate statistically significant differences ($p < 0.05$; n = 8)

Table 5: Biochemical profile of diabetic rats treated with glibenclamide and different doses of a Thai herbal extract

Group	Blood chemistry parameters in normal and STZ-induced diabetic rats							
	Renal function		***Liver functions***					
	BUN (mg/dL)	***Cr (mg/dL)***	***AST (U/L)***	***ALT (U/L)***	***ALP (U/L)***	***TG (mg/dL)***	***TC (mg/dL)***	***HDL (mg/dL)***
NM-Control	17.00±1.87[a]	0.26±0.05[a]	104.00±21.62[a]	43.20±13.05[a]	123.80±25.43[a]	75.00±30.02[a]	53.20±13.33[a]	33.00±9.30[a]
DM-Control	39.20±4.67[b]	0.18±0.04[a]	360.00±15.95[c]	248.00±15.12[c]	440.60±23.92[b]	154.00±36.77[b]	131.00±74.34[c]	56.80±13.05[b]
DM-GB	32.83±4.26[b]	0.15±0.05[a]	305.00±13.34[c]	255.67±12.80[c]	545.33±26.49[b]	260.33±22.67[c]	97.83±32.21[b]	52.50±10.77[b]
DM-125	28.83±4.88[b]	0.18±0.04[a]	204.50±13.77[b]	113.50±22.55[b]	426.17±51.48[b]	132.83±42.57[b]	87.00±14.89[b]	58.83±8.73[b]
DM-250	32.33±8.33[b]	0.18±0.04[a]	223.67±12.79[b]	108.67±18.35[b]	374.33±12.15[b]	166.80±11.36[b]	115.67±68.79[c]	54.83±6.40[b]
DM-500	29.57±5.74[b]	0.20±0.00[a]	227.00±13.14[b]	125.29±13.82[b]	442.14±22.91[b]	162.86±16.75[b]	88.43±19.58[b]	54.43±15.65[b]

The mean values followed by distinct uppercase letters (a, b, c) within the same columns indicate statistically significant differences ($p < 0.05$; n = 8)

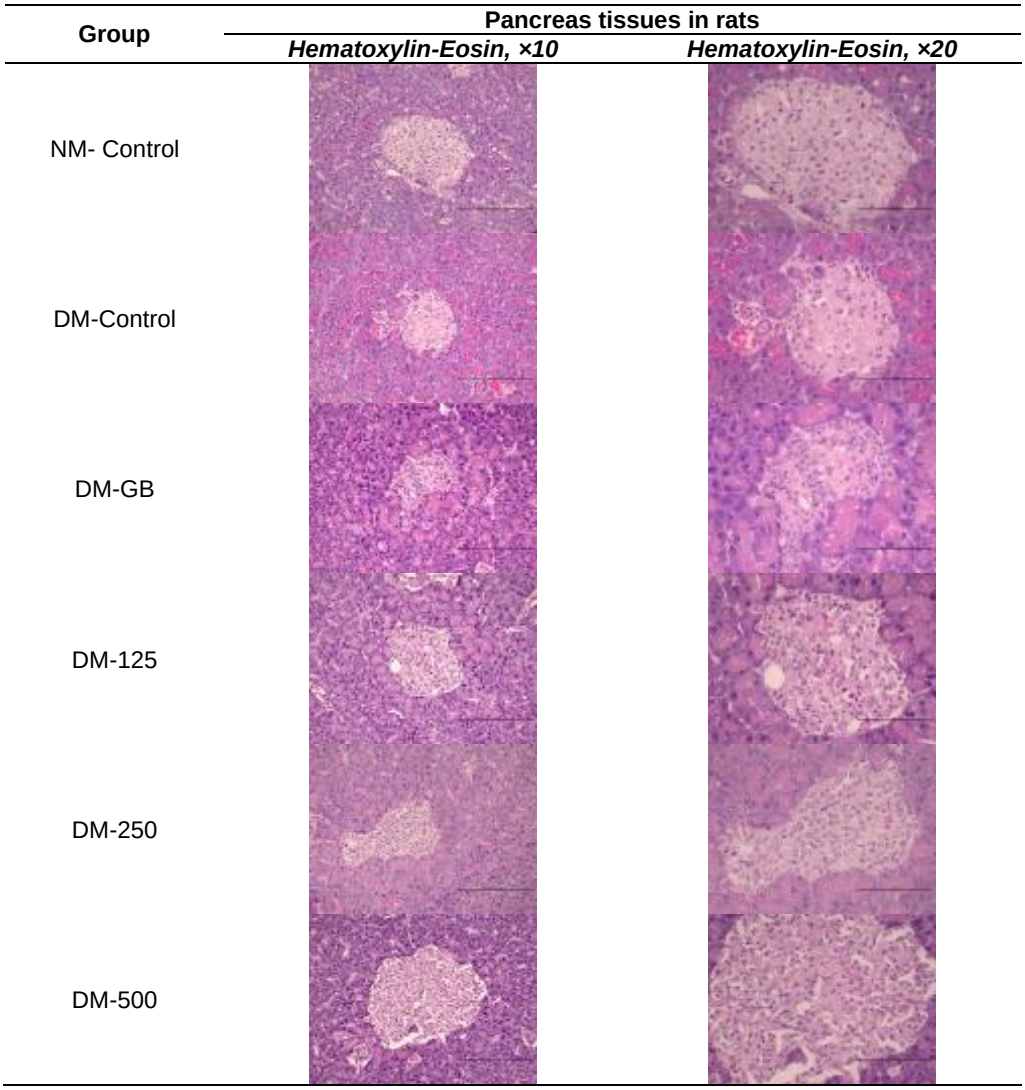

Figure 1: Histopathological illustration of pancreas tissues in normal and streptozotocin-induced diabetic rats treated with glibenclamide and different doses of a Thai herbal extract (×10 and × 20, scale bar = 200 and 100 µm, respectively)

DISCUSSION

This study elucidates the substantial hypoglycemic effects of a traditional Thai seven-herb formula on streptozotocin-induced diabetic rats, demonstrating its potential as an adjunct therapy in diabetes management. The aqueous extract conspicuously reduced fasting blood glucose levels, with the most significant decrease observed by the 250 mg/kg dose, aligning with findings from Salehi *et al* [12], who also reported glucose-lowering effects using a different Thai herbal combination. Such dose-dependent responses are supported by Kumar *et al* [14], emphasizing the importance of pinpointing optimal dosages to maximize efficacy and minimize adverse effects. Moreover, the extract's influence on body weight gain in diabetic rats suggests its role in counteracting diabetes-related weight loss, potentially due to enhanced glycemic control and improved insulin sensitivity, as Pandey *et al* [13] have indicated. The multi-herb configuration of the formula may exert a synergistic effect that simultaneously tackles various facets of diabetes pathophysiology.

A notable reduction in HbA1c levels among treated groups indicates improved long-term glycemic control, aligning with Stohs and Ray's observations [11] of similar impacts with components like Salacia species present in our formula. Such reductions are crucial for minimizing the risk of diabetic complications. Enhancements in lipid profiles and liver function markers further suggest that the herbal formula could extend benefits beyond glucose regulation, possibly providing hepatoprotective effects critical for diabetic patients, who are at increased risk for liver disease, as noted by Ota and Ulrih

[2]. Furthermore, histopathological examinations revealed a dose-dependent restoration of pancreatic islet structure, suggesting potential protective or regenerative effects on pancreatic β-cells. This finding echoed in Scudamore [19], highlights the formula's possible implications for long-term diabetes management and its ability to possibly delay disease progression, offering a comprehensive approach to tackling diabetes at multiple physiological levels.

Findings regarding the safety profile of herbal extract are promising, showing no signs of acute toxicity. However, it is crucial to conduct long-term safety studies to fully ascertain the extract's safety, as emphasized by Choudhury *et al* [15], who advocate for rigorous safety assessments in developing herbal medicines, especially for chronic conditions like diabetes. The holistic approach of traditional Thai medicine is reflected in the use of multiple herbs in this study. Each herb contributes unique bioactive compounds that potentially work synergistically, enhancing the overall therapeutic effect. For example, *Clerodendrum paniculatum* is known for its antioxidant properties, which may mitigate diabetes-induced oxidative stress [5], while *Arcangelisia flava* contains berberine, renowned for its glucose-lowering effects [6]. This synergistic combination offers a more comprehensive diabetes management strategy compared to single-herb treatments.

Despite the encouraging outcomes, the limitations of our study must be acknowledged. The brief duration and reliance on a single animal model restrict the generalizability of our findings. Future research should include longer treatment durations and multiple animal models to validate these results further. Human clinical trials are imperative to confirm the efficacy and safety of this herbal formula in diabetic patients. Moreover, the exact mechanisms of action and identification of the active compounds responsible for the observed effects are yet to be determined. Wanchai and Phrompayak [3] suggest that further phytochemical analyses and in vitro studies are necessary to pinpoint these bioactive components and their molecular targets. A deeper understanding of these mechanisms could facilitate the development of more precise and effective herbal diabetes treatments. Lastly, the potential for herb-drug interactions must be considered, particularly if this herbal formula is used alongside conventional diabetes medications. Neamsuvan *et al* [10] underline the importance of exploring these interactions to ensure the safe and effective integration of herbal treatments with established diabetes therapies. This aspect is critical for minimizing adverse effects and enhancing patient outcomes in the use of traditional herbal formulations in modern medical contexts.

CONCLUSION

This study has examined the hypoglycemic activity of an aqueous extract from a traditional Thai herbal formula on streptozotocin-induced diabetic rats. The findings support the anti-diabetic potential of this traditional Thai herbal formula. The significant improvement observed in glucose regulation, metabolic health, and pancreatic histology demonstrates the formula's potential as a valuable adjunct in managing diabetes. However, to firmly establish its efficacy and safety for human use, clinical trials are essential.

This study enriches the existing literature, stressing the potential of integrating traditional herbal medicines into contemporary diabetes care, thereby offering a more holistic approach to managing this chronic disease. These findings pave the way for further exploration and integration of herbal treatments, potentially enhancing diabetes management strategies worldwide.

DECLARATIONS

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Ethical approval

The protocol was approved by the Institutional Animal Care and Use Committee of Khon Kaen University (approval no. IACUC-KKU-67/2020).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the author(s) named in this article, and all liabilities

pertaining to claims relating to the content of this article will be borne by the authors.

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