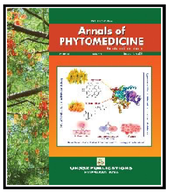
Annals of Phytomedicine 14(1): 608-621, 2025

DOI: http://dx.doi.org/10.54085/ap.2025.14.1.58

Annals of Phytomedicine: An International Journal

http://www.ukaazpublications.com/publications/index.php

Print ISSN : 2278-9839 Online ISSN : 2393-9885



Original Article : Open Access

Evaluation of antidiabetic activity of an Unani herbomineral formulation in nicotinamide streptozotocin induced diabetic rats

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Article Info

Article history

Received 1 April 2025

Revised 13 May 2025

Accepted 14 May 2025

Published Online 30 June 2025

Keywords

Antidiabetic activity

Diabetes mellitus

Dawwariyya

Dhayabitus

Dulabiyya

Herbomineral formulation

Parkariyya OGTT

Streptozotocin

Unani

Ziabetus

Abstract

Diabetes mellitus (DM) is one of the most common metabolic disorders, with more than 589 million documented cases. The management of DM is costly and also have a number of side effects. Its management falls short because there is no permanent cure and patients must take medicine for the rest of their lives. Keeping these perspectives in mind, a Unani herbomineral formulation (HMF) was assessed for its antidiabetic activity and safety. The aim was to validate the claim made by traditional Unani physicians about its antidiabetic effects. Antidiabetic effect of HMF was investigated in rats. The oral glucose tolerance test (OGTT) was performed to evaluate peripheral glucose utilization, and antihyperglycemic activity was evaluated using nicotinamide streptozotocin (STZ-Nic.) induced diabetes rat model. HMF markedly reduced blood glucose levels during the OGTT for up to 60 min at a dosage of 1400 mg/kg. Fasting BG levels significantly decreased after HMF treatment in STZ-Nic. induced diabetic rats at 14th and 28th day of treatment at both tested doses. The findings of present investigation validate the ethnopharmacological use of this traditional Unani formulation for management of diabetes.

1. Introduction

DM is primarily characterized by chronic hyperglycaemia. Impairments in insulin secretion, insulin action, or both are usually to blame (Petersmann *et al.,* 2019). DM is a prevalent, although potentially catastrophic, medical disorder that has risen in incidence over recent decades, presenting a significant public health challenge in the twenty-first century (Zimmet *et al.,* 2001). Globally, 589 million persons aged 20-79 have diabetes. By 2050, this figure is supposed to be 853 million. In 2024, diabetes was the cause of 3.4 million deaths. At least $1 trillion was spent on diabetes-related medical care, a 338% rise over the previous 17 years (IDF, 2025). In 2030, five Asian countries (China, India, Pakistan, Indonesia, and Bangladesh) are expected to have the maximum prevalence of DM (Shaw *et al.,* 2010).

DM has been acknowledged since antiquity. The Egyptian papyri, ancient Chinese, Indian medical manuscripts, and Greek and Arab physicians, described the disease (Karamanou, 2016). Avicenna (Ibn Sina), the renowned Unani physician, documented abnormal hunger and gangrene in diabetic patients, and formulated a treatment of seeds of fenugreek, zedoary, and lupin (Sina, 2010). The Macrovascular problems, such as coronary heart disease, stroke, and peripheral artery disease while microvascular such as renal disease, retinopathy, and peripheral neuropathy has been associated with diabetes (Fowler, 2008). Asia has become the global 'diabetes hotspot' due to rapid economic expansion, urbanization and nutrition transitions in recent years (Chan *et al.,* 2009).

Diabetes (ziabetus) is also called as dhayabitus, dûlâbiyya, muattisha, dawwâriyya, and parkâriyya. The Unani medicine asserts that diabetes is a renal disorder arising from an increase in the excessively hot temperament (Su'-Mizaj-i-Harr). A heated temperament compromises renal function and diminishes the retentive capacity of kidney (Quwwat mâsika), resulting in excessive fluid discharge. The morbid temperament exacerbates the body's absorptive faculty (Quwwat jadhiba). Due to diminished retentive faculty and increased expulsive faculty (Quwwat dafia), absorptive faculty extracts and absorbs a disproportionate quantity of liquid from the liver while neglecting to hold and digest it; ultimately, the fluid proceeds to the urinary bladder and is excreted in substantial volumes (Sina, 2010; Qurshi, 2022). Unani physicians have been treating DM since ancient times. They have detailed a variety of single and polyherbal medications for managing the condition. Various compound formulations and individual medications have been utilized for the treatment of diabetes mellitus, including Qurs Tabasheer and Qurs Kafoor, among others (Majusi, 2010).

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Various natural secondary metabolites (phytochemicals) demonstrate significant potential for the development of commercially viable and effective antidiabetic pharmaceuticals for clinical use (Anwar *et al.*, 2024). Flavonoids, terpenes, alkaloids, stilbenes, and tannins are phytochemicals acknowledged for their protective potential against diabetic neuropathy. The compounds possess the capability to affect various cellular pathways involved in the development and progression of neuropathy, including the reduction of oxidative stress and inflammation, along with promoting nerve growth and repair (Hashim *et al.,* 2024).

The medical industry is still grappling with controlling diabetes mellitus without causing side effects because conventional diabetes medications have several adverse effects. The traditional medicines used to treat diabetes do not fully meet the need; new antidiabetic pharmaceuticals are urgently needed to address this issue. Given this urgency, finding new antidiabetic medication is crucial for addressing this issue. An Unani herbomineral formulation (HMF) was chosen to assess its potential for antidiabetic effects. The HMF has twelve ingredients; Tabasheer (*Bambusa bambos* (L.) Voss (18 g), Rub-us-soos (*Glycyrrhiza glabra* L.) (18 g), Tukhm hummaz (*Rumex vesicarius* L.) (35 g), Kishneez khushk (*Coriandrum sativum* L.) (35 g), Gile armani (*Arminia bole*) (35 g)*,* Tukhm kahu (*Lactuca sativa* L.) (52.5 g), Tukhm khurfa (*Portulaca oleracea* L.) (52.5 g), Sandal safed (*Santalum album* L.) (10.5 g), Gulnar (*Punica granatum* L.) (10.5 g), Sumaq (*Rhus coriaria* L.) (10.5 g), Gond babool (*Acacia nilotica* L.) Delile (10.5 g), Kafoor (*Cinnamomum camphora* (L.) J. Presl.) (1.75 g) (Khan, 1944). Eminent Unani physicians prescribe Mujarrabât (practices or treatments that have been tried and found effective) as a therapy for diabetes mellitus. Unani literature suggests that components of HMF have antidiabetic properties and preclinical research in *in vivo* models have confirmed few of them. Due to a lack of scientific data, the efficacy of HMF in STZ-Nic. induced diabetes mellitus was examined based on scientific parameters to substantiate indications mentioned in Unani literature.

However, the HMF has been used clinically for so many years successfully; it was chosen to analyze scientific parameters for establishing its reverse pharmacology. The formulation was assessed for its efficacy and safety in diabetic rats. The selection for combination therapy (STZ-Nic.) is based on the finding by Szkudelski T, 2012 to create a model with moderate hyperglycemia which mimics type 2 diabetes (Szkudelski, 2012).

2. Materials and Methods

2.1 Plant ingredients and preparation of formulation

All ingredients of the formulation were obtained from the Hyderabad regional marketplace and validated by Dr. Mohd Kashif Husain, RO (Botany), Incharge of SMP Unit, NRIUMSD Hyderabad. The Voucher Specimens, SMPU/CRI-Hyd-15849; 15850; 15851; 15852; 15853; 15854; 15855; 15856; 15857; 15858 and 15859, for *B. bambos* (L.) Voss.; *G. glabra* L.; *R. vesicarius* L.; *C. sativum* L.; *L. sativa* L.; *P. oleracea* L.; *S. album* L.; *P. granatum* L.; *R. coriaria* L.; *A. nilotica* L. Delile and *C. camphora* (L.) J. Presl., respectively, were preserved. The formulation was prepared in the pharmacy department of NRIUMSD, Hyderabad, as per the general method of preparation mentioned in NFUM (NFUM, 2007).

2.2 TLC and HPTLC fingerprinting

Two grams of HMF powders were extracted using 20 ml of ethanol in an ultrasonicator for 30 min at 45°C, with the procedure conducted in duplicate. The extracts were filtered using Whatman No. 1 and 41 filter papers and subsequently transferred to vials for analysis (Akram *et al.,* 2024).

2.2.1 Chromatographic conditions

Twenty microliters (20 µl) of the ethanol extract of HMF was applied as an 8 mm band on 20 cm × 10 cm silica gel 60 F254 HPTLC plates, utilizing an automatic TLC sampler 4 (ATS4, CAMAG). A solvent mixture including toluene, ethyl acetate, and formic acid (8.0: 2.0: 0.01, v/v/v) was employed for 20 min of saturation in a vertical twin trough chamber, and the samples were examined at 254 nm and 366 nm using a TLC visualizer. The plate underwent derivatization using a vanillin sulfuric acid reagent, followed by scanning at 254 nm and 366 nm UV in absorption and fluorescence modes, respectively (Akram *et al.,* 2024).

2.3 Animals

In this experiment, SD male rats (180-200 g; age: 8-10 weeks) were used. The ICMR-NIN, Hyderabad provided the animals. Standard laboratory conditions were maintained (12/12 hrs light/dark, Temp: 22°C ± 3°C, RH: 30-70%). The animals were placed in polycarbonate cages with grain (corn cob) bedding in groups of six. The rats were allowed a week to acclimate to the laboratory setting before being utilized in experiments. The experimental approach adhered to the requirements set by CCSEA and received approval from the IAEC with Registration No. NRIUMSD/IAEC/19/2023/01/P01 on 18/03/2023.

2.4 Experimental methodology

The animal dose of HMF was established through allometric dose conversion for rats, utilizing body surface area as a basis (Reagan Shaw *et al.,* 2008). HMF has a dosing range of 7 g daily, according to Unani literature. The animal dose was determined to be 700 mg/kg bw. Furthermore, 1400 mg/kg as a second dose was used to see the effect of different doses. The fine powder of HMF was suspended in 0.3% aqueous suspension of carboxyl methylcellulose (CMC). Low and high dosages were made by mixing 10 ml of 0.3% CMC with 700 mg of HMF powder and 20 ml of 0.3% CMC with 1400 mg of HMF powder, respectively. Streptozotocin was dissolved in ice-cold citrate buffer (pH; 4) and administered once intraperitoneally at a dose of 65 mg/kg. After 15 min of STZ administration nicotinamide (120 mg/kg) was administered intraperitoneally. Every day, a fresh suspension of HMF was prepared. The suspension was administered through a stainless-steel feeding cannula after being homogenized for a minute by vigorous shaking.

2.4.1 Experimental design for OGTT

The OGTT procedure was performed to determine how much glucose was used in the peripheral tissues. It assesses how well the body handles glucose uptake and utilization following an oral glucose load, primarily to diagnose or screen for conditions like impaired glucose tolerance and type 2 diabetes. Rats were randomized into four groups (n = 6) and fasted for 24 h before being given the drug (Table 1).

Table 1: Treatment schedule for OGTT

Groups	Treatment
Vehicle control	Rats were given the 0.3% CMC suspension orally.
Glibenclamide 10 mg/kg	Rats were given glibenclamide (10 mg/kg) orally.
HMF 700 mg/kg	Rats were given 700 mg/kg of HMF powder orally.
HMF 1400 mg/kg	Rats were given HMF powder (1400 mg/kg) orally.

After the HMF powder and glibenclamide treatments, glucose (2 g/kg) was given orally 30 min later. Blood samples were taken before glucose dose and at 30, 60, and 120 min after glucose dose to measure BG levels (Husain *et al.,* 2009; Dwivedi and Jena, 2023).

2.4.2 Experimental design for STZ-Nic. induced diabetes model

A total 5 groups were randomly created having 6 rats in each group. Prior to commencing the trial, all animals had an overnight fasting period. During the experiment, the body weight of rats was measured and diabetes was induced by injecting streptozotocin (65 mg/kg; i.p.) and nicotinamide (120 mg/kg; i.p.) within 15 min after STZ in four groups, one group of six animals was left to serve as vehicle control. After 10 days of inductions, blood samples were withdrawn from the retro-orbital plexus, and fasting BG was estimated in all rats using a glucometer (ACCU-CHEK active). Rats found with steady hyperglycemia (FBG ~ 200 mg/dl) were taken for further study, and the following dose regimen was given in Table 2 (Masiello *et al.,* 1998).

Table 2: Treatment schedule for STZ-Nic. induced diabetes model

Groups	Treatment
Vehicle control	0.3% CMC suspension was orally given from 10^{th} day onward for 28 days.
STZ-Nic. control	0.3% CMC suspension was orally given from 10^{th} day onward for 28 days.
STZ-Nic. + Glibenclamide 10 mg/kg	Glibenclamide (10 mg/kg) was orally given from 10^{th} day onward for 28 days.
STZ-Nic. + HMF 700 mg/kg	HMF (700 mg/kg) was orally given from 10^{th} day onward for 28 days.
STZ-Nic. + HMF 1400 mg/kg	HMF (1400 mg/kg) was orally given from 10^{th} day onward for 28 days.

2.4.3 Blood collection for biochemical and hematological analysis

After completion of the experiment (day 28), 2-3 ml of blood was withdrawn from the retro-orbital plexus under isoflurane inhalation (EZ anaesthesia system) for biochemical estimation in serum. The biochemical kits for bilirubin, ALT, AST, ALP, glucose, urea, creatinine, total cholesterol, triglycerides, HDL, LDL, total protein and albumin were procured from Erba Mannheim (Transasia Pvt. Ltd.). The hematological analysis was done by using veterinary hematology analyzer (Nihon Kohden India Pvt. Ltd.). Immediately after the collection of blood samples, animals were euthanized under carbon dioxide asphyxia and gross necropsy was carried out. Liver, kidney, and pancreas were isolated and processed for histological examination.

2.4.4 Statistical analysis

The information provided was expressed as mean ± standard error mean (SEM). After examining the mean variance among the control and medication categories utilizing an ANOVA with a one-way design, Tukey's numerous comparisons were conducted employing Graph Pad Prism (version 5). A statistically significant p value was defined as a value below 0.05.

3. Results

3.1 HPTLC fingerprinting of HMF

The HPTLC fingerprinting confirmed the presence of diverse phytochemical constituents in the ethanol extract of HMF, detected under two distinct ultraviolet (UV) wavelengths. Under UV light at 254 nm, seven prominent peaks were recorded at Rf values of 0.02 (56.31%), 0.13 (3.55%), 0.19 (3.74%), 0.27 (2.05%), 0.43 (17.79%), 0.49 (7.76%), and 0.94 (8.79%). At 366 nm, eight major peaks were identified with Rf values of 0.01 (1.53%), 0.04 (36.46%), 0.15 (8.04%), 0.24 (20.88%), 0.48 (6.49%), 0.60 (14.48%), 0.85 (7.20%), and 0.94 (2.92%), as presented in Table 3. These chromatographic profiles reflect a distinctive chemical fingerprint of the ethanol extract of HMF, characteristic of the solvent system employed. The fingerprinting results, supported by the 3D densitogram and corresponding Rf values illustrated in Figure 1, confirm the presence of active phytoconstituents within the extract. The comprehensive data obtained serve as an effective tool for the identification and characterization of phytoconstituents in HMF, providing a reliable reference for future studies (Christopher *et al.,* 2024).

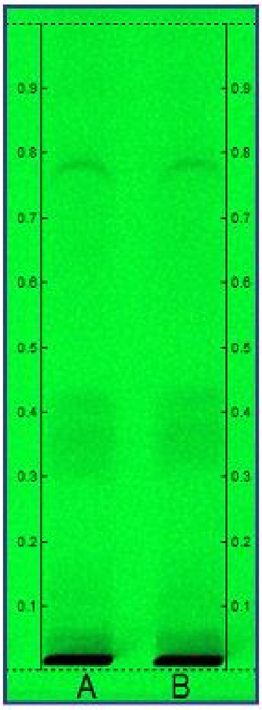
3.2 Effect of HMF on OGTT

The glibenclamide group have shown significant reduction in BG level at 30, 60 and 120 min as compared to vehicle control. The HMF at 700 mg/kg and 1400 mg/kg had lower BG level at 30, 60 and 120 min but the difference was not significant, only HMF at 1400 mg/kg dose, had significantly lower BG levels at 60 min (*p<0.05) (Figure 2).

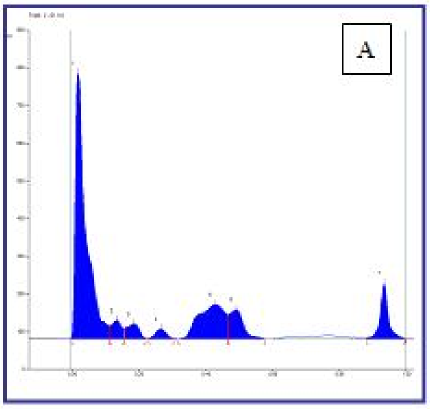
Table 3: Rf values of ethanolic extract of HMF

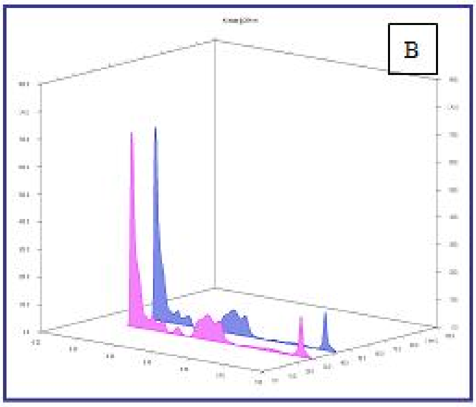
UV - 254 nm		UV - 366 nm	
Rf	Colour	Rf	Colour
0.02	G	0.01	LR
0.13	G	0.04	BL
0.19	G	0.15	LG
0.27	G	0.24	LB
0.43	G	0.48	BL
0.49	G	0.60	LR
0.94	G	0.85	LR
		0.94	BL

G = green; LR = light red; BL = blue, LG = light grey; LB = light blue



UV – 254 nm





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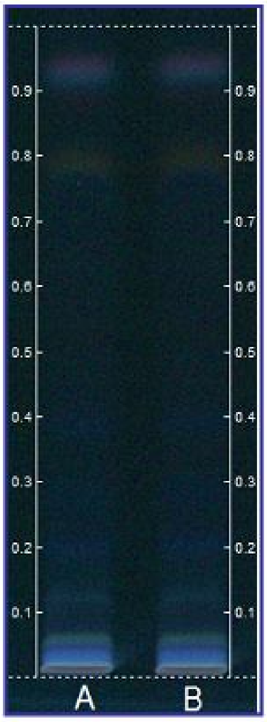
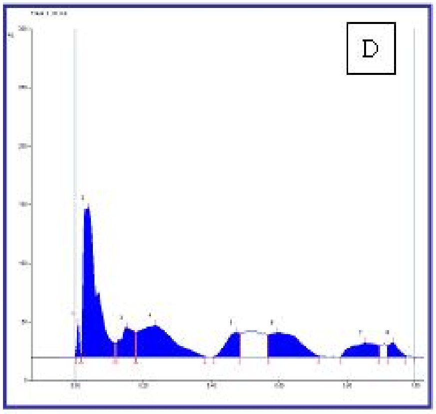
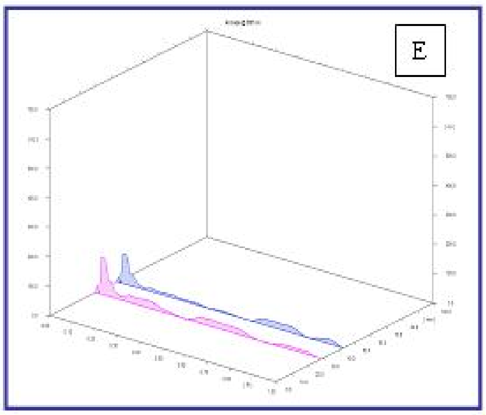
Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	-0.00 Rf	3.6 AU	0.02 Rf	704.7 AU	62.14 %	0.11 Rf	34.8 AU	16547.9 AU	56.31 %
2	0.11 Rf	34.9 AU	0.13 Rf	48.8 AU	4.30 %	0.15 Rf	26.9 AU	1044.4 AU	3.55 %
3	0.16 Rf	26.9 AU	0.19 Rf	38.6 AU	3.40 %	0.22 Rf	2.6 AU	1098.0 AU	3.74 %
4	0.23 Rf	1.9 AU	0.27 Rf	26.0 AU	2.29 %	0.30 Rf	0.5 AU	603.7 AU	2.05 %
5	0.32 Rf	0.1 AU	0.43 Rf	90.8 AU	8.01 %	0.47 Rf	64.3 AU	5226.9 AU	17.79 %
6	0.47 Rf	64.5 AU	0.49 Rf	78.1 AU	6.89 %	0.58 Rf	0.1 AU	2281.2 AU	7.76 %
7	0.88 Rf	2.7 AU	0.94 Rf	147.0 AU	12.96 %	1.00 Rf	0.5 AU	2583.2 AU	8.79 %

A) HPTLC finger print of HMF in alcohol extract at 254 nm,
B) 3D Densitometry chromatogram of HMF in alcohol extract at 254 nm,
C) Peak table of HMF in alcohol extract at 254 nm



UV – 366 nm





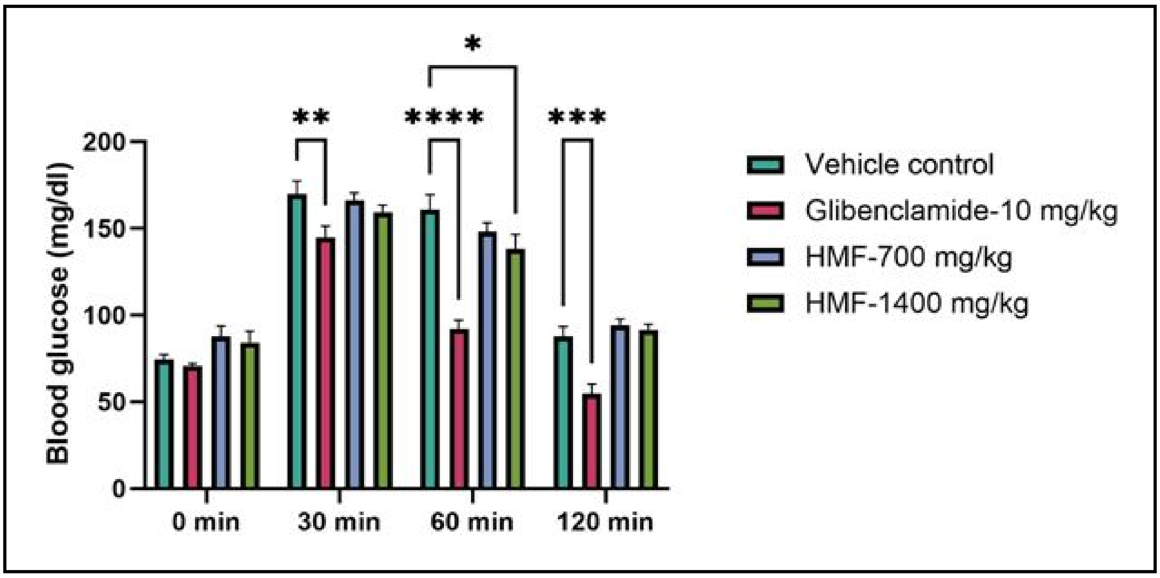
F

Track 2, ID: KA

Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.00 Rf	1.6 AU	0.01 Rf	28.4 AU	10.35 %	0.02 Rf	1.1 AU	142.1 AU	1.53 %
2	0.02 Rf	6.3 AU	0.04 Rf	127.4 AU	46.40 %	0.12 Rf	12.3 AU	3583.3 AU	38.46 %
3	0.12 Rf	12.2 AU	0.15 Rf	25.3 AU	9.21 %	0.18 Rf	21.6 AU	749.4 AU	8.04 %
4	0.18 Rf	21.6 AU	0.24 Rf	27.0 AU	9.85 %	0.38 Rf	0.4 AU	1944.8 AU	20.88 %
5	0.41 Rf	0.4 AU	0.48 Rf	21.0 AU	7.64 %	0.49 Rf	20.5 AU	604.6 AU	6.49 %
6	0.57 Rf	19.2 AU	0.60 Rf	20.9 AU	7.61 %	0.72 Rf	1.2 AU	1349.1 AU	14.48 %
7	0.78 Rf	0.2 AU	0.85 Rf	12.0 AU	4.37 %	0.90 Rf	9.9 AU	670.5 AU	7.20 %
8	0.92 Rf	9.9 AU	0.94 Rf	12.6 AU	4.58 %	0.98 Rf	1.3 AU	272.4 AU	2.92 %

A) HPTLC finger print of HMF in alcohol extract at 366 nm,
B) 3D Densitometry chromatogram of HMF in alcohol extract at 366 nm,
C) Peak table of HMF in alcohol extract at 366 nm

Figure 1: HPTLC fingerprinting of ethanolic extract of HMF.

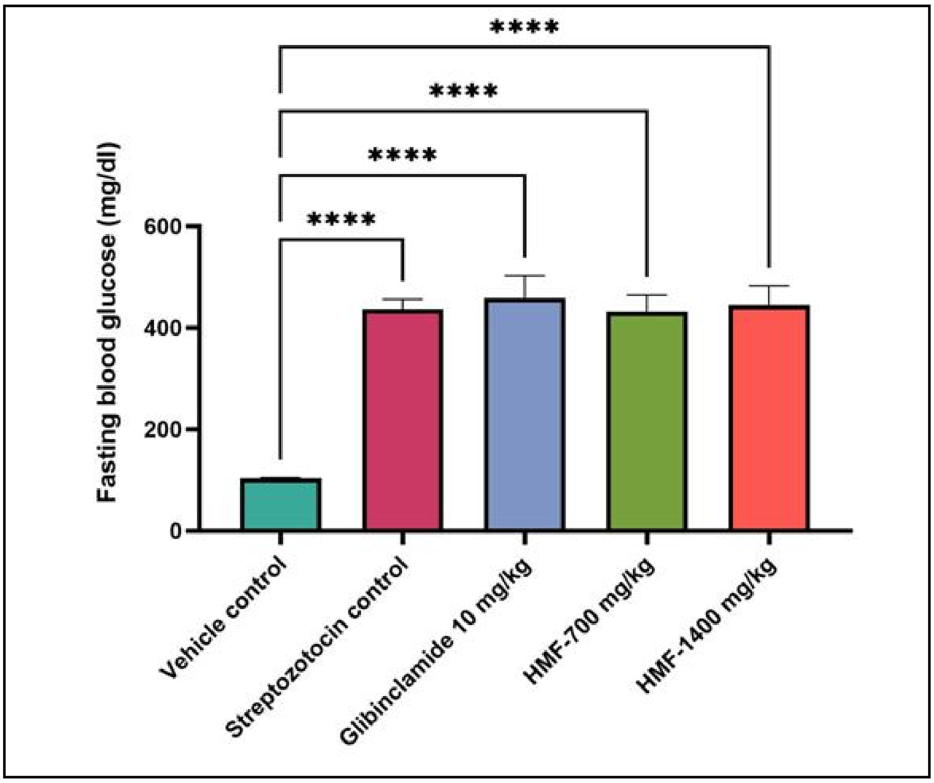


*$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$ vs. Vehicle control group.

Figure 2: Effect of HMF on OGTT.

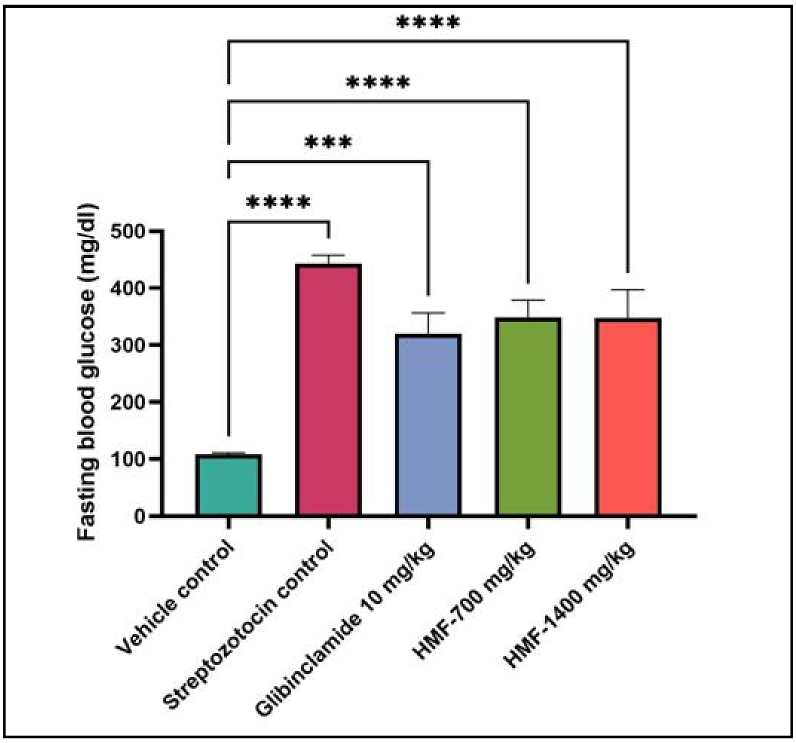
3.3 Effect of HMF on BG levels

A significant increase (***$p<0.001$) of BG level, (436.6 ± 19.74) in STZ-Nic. control group, (459.4 ± 43.25) in Glibenclamide control group, (432.4 ± 32.52) in HMF-700 mg/kg, and (445.4 ± 37.12) in HMF-1400 mg/kg was observed after 10 days of the treatment with STZ-Nic. (day-0) as compared to vehicle control group (103.4 ± 1.32) where STZ-Nic. was not given. After 14 days of treatment, the BG was decreased in all treatment groups but the results were not statistically significant vs. STZ-Nic. control group. The significant decrease in BG was seen in Glibenclamide control group, (263.0 ± 25.42; $p<0.001$), in HMF-700 mg/kg, (329.9 ± 43.79; $p<0.05$) and in HMF-1400 mg/kg (267.2 ± 40.86; $p<0.001$) as compared with STZ-Nic. control group after 28 days of treatment (Figures 3,4,5).



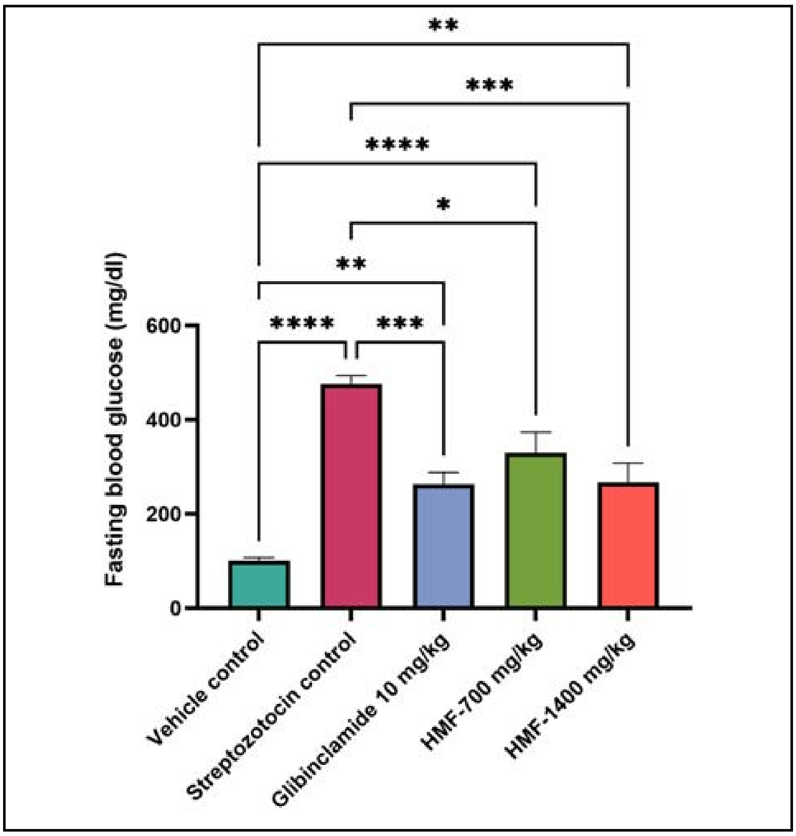
****$p<0.0001$ vs. Vehicle control group.

Figure 3: BG level in experimental rats on Day 0.



***p<0.001, ****p<0.0001 vs. Vehicle control group.

Figure 4: BG level in experimental rats on Day 14.



*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 vs. Vehicle control group.

Figure 5: BG level in experimental rats on Day 28.

3.4 Effect of HMF on liver function test

Result indicated that readings were seen high in total bilirubin, ALT, AST, ALP of all groups treated with STZ-Nic compared to vehicle control group. No statistically significant decrease was seen in total bilirubin, ALT, AST, ALP level in any treated group vs. STZ-Nic animals. Even though there is a slight decrease in AST, ALP levels in HMF 1400 mg/kg compared to STZ-Nic control group, it is statically insignificant (Table 4).

Table 4: Effect of HMF on liver function test

Groups	Bilirubin (mg/dl)	ALT (IU/l)	AST (IU/l)	ALP (IU/l)
Vehicle control	0.098 ± 0.00	42.49 ± 2.68	110.7 ± 5.33	107.0 ± 12.16
STZ-Nic. control	0.24 ± 0.04	109.3 ± 19.79	196.7 ± 29.64	921.4 ± 204.2
Glibenclamide 10 mg/kg	0.37 ± 0.06	152.4 ± 28.89	238.4 ± 67.68	1085 ± 147.4
HMF 700 mg/kg	0.34 ± 0.04	159.7 ± 24.95	259.6 ± 41.34	1186 ± 267.6
HMF 1400 mg/kg	0.39 ± 0.01	108.0 ± 16.80	126.2 ± 15.96	793.8 ± 198.0

3.5 Effect of HMF on renal function test

There was a significant increase in blood urea following STZ-Nic. treatment in all groups vs. untreated vehicle control. There was no significance difference in urea in any treated group compared to STZ-Nic. control group suggesting lack of reversal of rise in blood urea. No significant changes were observed in creatinine level compared to vehicle control or STZ-Nic. control (Table 5).

Table 5: Effect of HMF on renal function test

Groups	Urea (mg/dl)	Creatinine (mg/dl)
Vehicle control	30.76 ± 2.408	0.48 ± 0.02
STZ-Nic. control	92.66 ± 15.94	0.58 ± 0.02
Glibenclamide 10 mg/kg	100.6 ± 10.63	0.52 ± 0.02
HMF 700 mg/kg	121.5 ± 13.59	0.51 ± 0.04
HMF 1400 mg/kg	131.1 ± 12.55	0.48 ± 0.044

3.6 Effect of HMF on lipid profile

There was no noticeable distinction in total cholesterol, triglycerides, and HDL in any treated group compared to STZ-Nic. group while a significant decrease in LDL was seen in HMF 700 mg/kg and HMF 1400 mg/kg vs. STZ-Nic. control group ($p<0.05$), and readings persisted within standard physiological parameters (Table 6).

Table 6: Effect of HMF on lipid profile

Groups	Total cholesterol (mg/dl)	Triglycerides(mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Vehicle control	69.0 ± 2.43	121.4 ± 6.89	33.56 ± 1.23	22.43 ± 1.42
STZ-Nic. control	101.5 ± 5.13	126.9 ± 13.73	52.51 ± 3.38	31.59 ± 1.57
Glibenclamide 10 mg/kg	88.0 ± 9.70	114.9 ± 32.72	47.23 ± 4.98	24.97 ± 3.502
HMF 700 mg/kg	75.4 ± 9.35	79.9 ± 18.38	40.38 ± 6.83	20.18 ± 2.73*
HMF 1400 mg/kg	78.4 ± 6.42	61.88 ± 12.96	42.82 ± 3.66	20.7 ± 2.36*

*$p<0.05$, vs. STZ-Nic. control group

3.7 Effect of HMF on serum protein

Total protein and albumin were not substantially different between either of the treatment groups and the STZ-Nic. group and readings persisted within standard physiological parameters (Table 7).

Table 7: Effect of HMF on serum protein

Groups	Total protein (g/dl)	Albumin (g/dl)
Vehicle control	5.97 ± 0.19	3.10 ± 0.03
STZ-Nic. control	5.26 ± 0.17	2.84 ± 0.06
Glibenclamide 10 mg/kg	5.05 ± 0.11	2.71 ± 0.05
HMF 700 mg/kg	4.67 ± 0.28	2.56 ± 0.19
HMF 1400 mg/kg	5.09 ± 0.16	2.84 ± 0.07

3.8 Effect of HMF on haematological parameters

There was no significance difference in haematological parameters in any treated group in comparison with STZ-Nic. group and readings persisted within standard physiological parameters (Table 8).

Table 8: Effect of HMF on haematological parameters

Groups	WBC 10^3/µl	RBC 10^6/µl	HB%	HCT%	MCV (fl)	MCH (pg)	MCHC (g/dl)	Platelets 10^3/µl
Vehicle control	12.07 ± 0.60	9.32 ± 0.27	16.87 ± 0.529	49.57 ± 1.10	52.71 ± 0.51	18.09 ± 0.354	34.17 ± 0.38	871.5 ± 145.7
STZ-Nic. control	9.088 ± 0.79	9.34 ± 0.134	16.06 ± 0.43	49.1 ± 0.85	51.61 ± 0.73	17.14 ± 0.36	33.69 ± 0.377	539.4 ± 59.0
Glibenclamide 10 mg/kg	8.433 ± 2.41	9.15 ± 0.343	15.97 ± 0.47	48.61 ± 1.28	53.35 ± 0.91	17.87 ± 0.59	33.18 ± 0.43	642.8 ± 69.26
HMF 700 mg/kg	8.38 ± 1.99	8.72 ± 0.18	16.1 ± 0.49	46.98 ± 1.22	53.86 ± 0.697	18.44 ± 0.36	34.26 ± 0.211	565.8 ± 52.64
HMF 1400 mg/kg	8.10 ± 0.91	8.81 ± 0.58	15.82 ± 0.88	45.92 ± 2.55	52.26 ± 0.64	18.0 ± 0.225	34.44 ± 0.09	568.4 ± 74.26

3.9 Effect of HMF on body weights

The results showed no appreciable variations in any group at day 0 (following the process of hyperglycaemia induction along with prior to the start of medication), however there was a tendency for all STZ-Nic. treated rats to have lower body weights than the untreated vehicle control. In comparison to the vehicle control, the STZ-Nic. control (*p<0.05) and all treated groups, standard group 10 mg/kg (**p<0.01), HMF-700 mg/kg (*p<0.05), and HMF-1400 mg/kg (**p<0.01) showed a marked decrease in body weights on day 7. The STZ-Nic. control (**p<0.01), standard control 10 mg/kg (***p<0.001), HMF-700 mg/kg (***p<0.001), and HMF-1400 mg/kg (***p<0.001) in all treated groups showed the similar pattern on day 14 in comparison to the vehicle control. In comparison to the vehicle control, the STZ-Nic. control (***p<0.001) and all groups receiving standard control 10 mg/kg (***p<0.001), HMF-700 mg/kg (***p<0.001), and HMF-1400 mg/kg (***p<0.001) showed a substantial drop in BW on day 21. When compared to the STZ-Nic. control, the group treated with standard control 10mg/kg (#p<0.05) showed a significant drop in BW on day 21, and exactly the same group cured on the 28th day. The STZ-Nic. control (***p<0.001) and all groups receiving treatment (standard control 10mg/kg (***p<0.001), HMF-700 mg/kg (***p<0.001), and HMF-1400 mg/kg (***p<0.001)) showed a substantial drop in body weights on day 28 of therapy vs. vehicle control group. According to these results, HMF and conventional standard control treatment do not significantly increase body weights (Table 9).

Table 9: Effect of HMF on body weights

Groups	Before treatment	After treatment			
	Day 0	Day 7	Day 14	Day 21	Day 28
Vehicle control	358.9 ± 4.74	369.9 ± 5.57	384.5 ± 6.43	409.0 ± 6.46	411.2 ± 8.57
STZ-Nic. control	331.4 ± 14.92	318.0 ± 14.4*	317.1 ± 12.0**	288.7 ± 17.68***	311.9 ± 17.34***
Glibenclamide 10 mg/kg	316.5 ± 7.32	302.6 ± 5.85**	284.7 ± 4.19***	230.1 ± 9.03***#	261.4 ± 8.801***
HMF 700 mg/kg	327.4 ± 10.42	306.7 ± 16.61*	276.2 ± 15.87***	263.6 ± 13.44***	270.1 ± 15.96***
HMF-1400 mg/kg	327.6 ± 13.55	305.3 ± 15.34**	273.2 ± 13.54***	280.8 ± 17.26***	266.9 ± 18.44***

*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 vs. vehicle control and #p<0.05 vs. STZ-Nic. control.

3.10 Effect of HMF on histology of the liver, pancreas and kidney

All animals in HMF-1400 group, 4/5 (80%) animals in HMF-700 group, 5/6 (83.3%) animals in STZ-Nic. group and glibenclamide group, and 2/6 (33.33%) animals in vehicle control had normal liver histology. 1/6 (16.6%) animal each in vehicle, glibenclamide, and STZ-Nic. group, 1/5 (20%) animal in HMF-700 had shown focal lobular inflammation (score-1 inflammation). 1/6 (16.6%) animal in vehicle had lobular/periportal inflammation (score-2 inflammation), 1/6 (16.6%) animal in vehicle had microvesicular steatosis (5-33%) (score-1 inflammation) and 1/6 (16.6%) animal in vehicle control group had microvesicular and macrovesicular steatosis with foci of inflammation (33-66%) (score-3 inflammation) (Figure 6).

All animals in glibenclamide group, 2/5 (40%) animals in HMF-700 and 2/5 (40%) animals in HMF-1400 group had normal number of islets cluster with normal numbers of islet cells in them with focal lymphocytes. 3/5 (60%) animals in HMF-700 and 3/5 (60%) animals in HMF-1400 group had slightly decreased number of Islet clusters with mild lymphocyte infiltration and few vacuolated cells. 4/6 (66.6%) animals in STZ-Nic. group had decreased number of Islets clusters (only 10% of section) with small size and infiltrated with lymphocytes and few dilated blood vessels. 2/6 (33.3%) animals in STZ-Nic. group had decreased number of Islets cell clusters (30-40% of section) with dilated vessels. 60% each of the animal of the HMF-700 and HMF-1400 had slightly decreased islets in pancreas (Figure 7).

Normal kidney histology was seen in 1/6 (16.6%) animal in STZ-Nic. group and 1/5 (20%) animal in HMF-1400 group. Severe degeneration with more than 80% degeneration with dilatation of proximal convoluted tubules (PCT) and distal convoluted tubules (DCT) and many showing clear cells lining the tubules, occasional to 50% tubules show grey-white globules in their lumen was seen in 2/6 (33.3%) animal in STZ-Nic. group. Moderate degeneration with

50-80% degeneration with dilatation of PCT and DCT and many showing clear cells lining the tubules, most of the tubules also contain grey-white globules in their lumen was seen in 3/6 (50%) animals in STZ-Nic., 1/6 (16.6%) animals in glibenclamide, 4/5 (80%) animals in HMF-700 and 3/5 (60%) animals in HMF-1400 group. Mild degeneration with less than 50% degeneration with dilatation of PCT and DCT and many showing clear cells lining the tubules, most of the tubules also contain globules in their lumen was seen in 1/6 (16.6%) animals in glibenclamide, and 1/5 (20%) animals in HMF-700 (Figure 8).

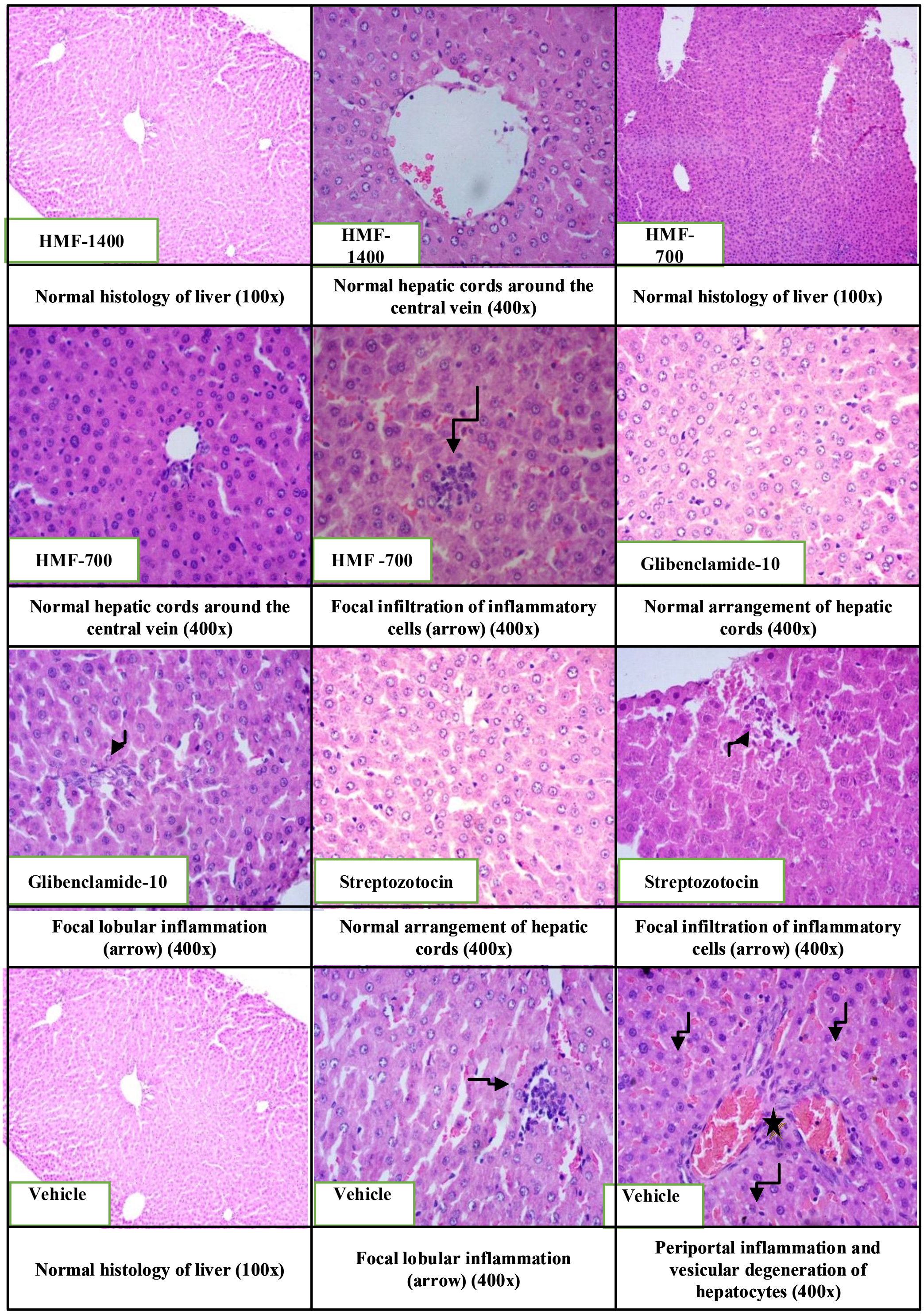
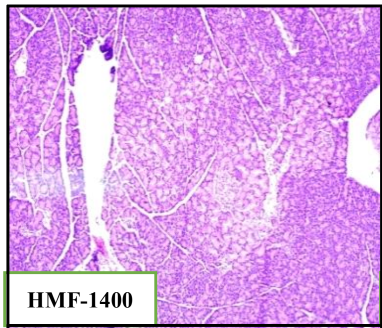
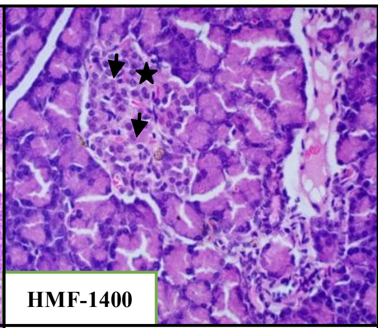


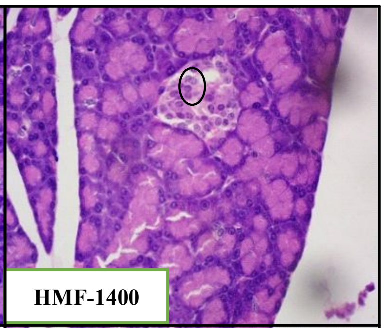
Figure 6: Photomicrograph showing histology of liver in various groups.



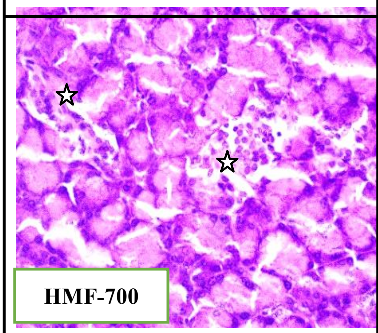
Normal histologic appearance of pancreas (100x)



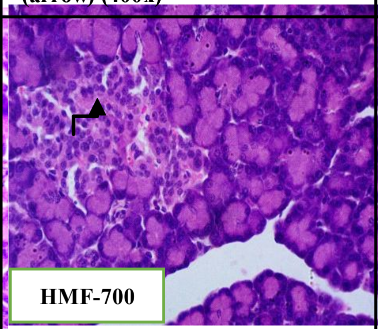
Normal no of islet cells in islet cluster (asterisk), lymphocyte (arrow) (400x)



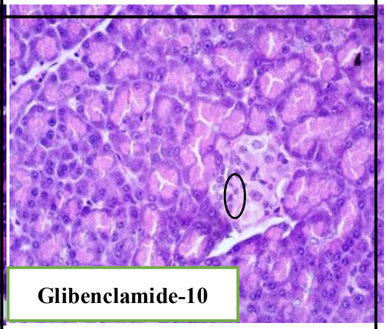
Slightly decrease in islet cells (circle) (400x)



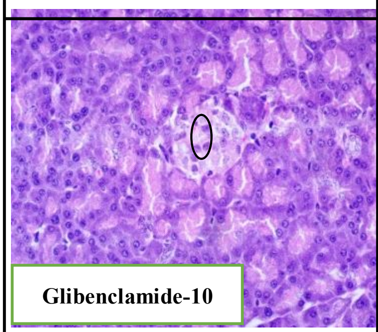
Slightly decrease in islet cells (asterisk) (400x)



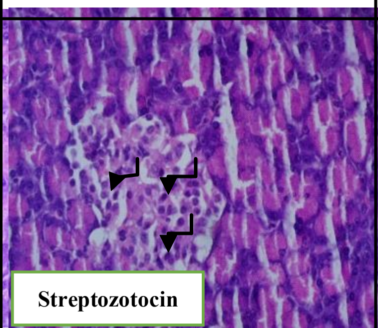
Normal no of islet cells (circle) in islet cluster (400x)



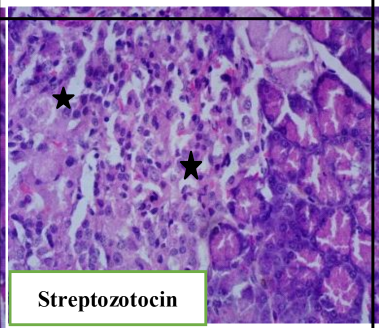
Normal no of islet cells (circle) in islet cluster (400x)



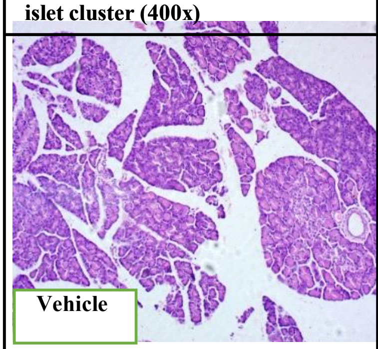
Normal no of islet cells (circle) in islet cluster (400x)



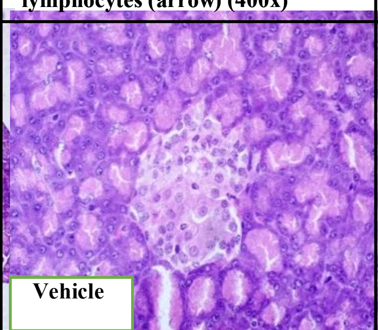
Very mild decrease in islets, focal lymphocytes (arrow) (400x)



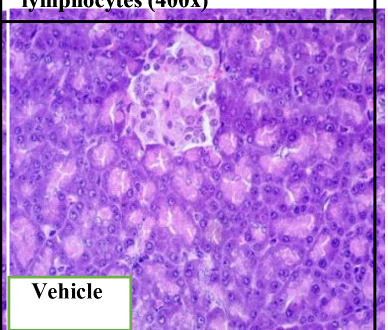
Mild decrease in islets, focal lymphocytes (400x)



Normal histology of Pancreas (100x)



Normal no of islet cells in islet cluster (400x)



Normal no of islet cells in islet cluster (400x)

Figure 7: Photomicrograph showing histology of pancreas in various groups.

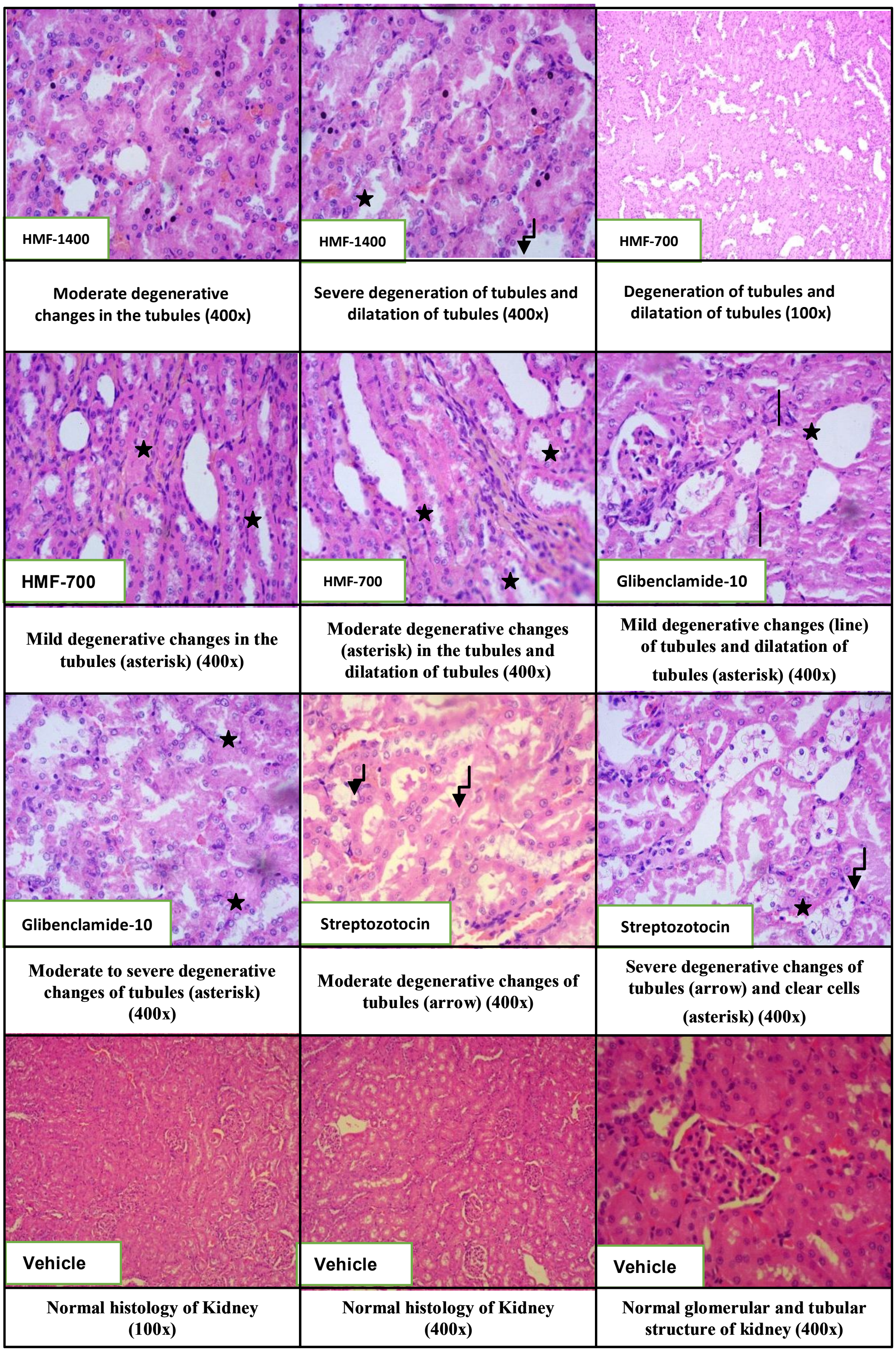


Figure 8: Photomicrograph showing histology of kidney in various groups.

4. Discussion

Almost half of the population with diabetes are unaware of the disease, and approximately 24 million individuals globally suffer with undetected diabetes. Globally, a total of 537 million individuals between the ages of 20-79 are thought to be suffering the illness at the moment. The prediction that the number of cases of DM will rise to 643 million by the year 2030 and 73 million (12.2%) by 2045 is concerning (Hossain *et al.,* 2024). But, the main concern is antidiabetic drugs have a lot of side effects like metformin is considered as a key of antidiabetic agent but it causes gastric disturbances like nausea, vomiting (Nabrdalik *et al.,* 2022), abdominal pain, bloating, *etc*. (Rayner *et al.,* 2001) and a precarious complication is lactic acidosis which is not seen in every case. Like metformin, other antidiabetic drug also creates a complicacy like hypoglycemia, hyperglycaemia, and flu-like symptoms (Pfeiffer *et al.,* 2014).

There are several studies on single herbs, natural bioactive chemicals and natural formulations to validate their antidiabetic activities. Impact of the ethanolic leaf extract of *Bunchosia glandulifera* in STZ-Nic.-induced diabetic rats demonstrated a statistically significant reduction in BG levels and an enhancement of glycogen storage in liver and muscle tissues. In *in vitro* tests, the ethanolic leaf extract of *B. glandulifera* significantly enhanced glucose absorption and glycogen storage in the tissue (Eshan *et al.,* 2024). An insilico study revealed that the natural compounds sesamin, kobusin, methylpluviatilol, planinin, piperitol, and saltillin demonstrated efficacy superior to that of standard drugs. The findings indicate that these compounds may serve as potential drug candidates for the activation of peroxisome proliferator-activated receptor gamma. This study aimed to identify a novel drug derived from natural plants that can activate peroxisome proliferator-activated receptor gamma without adverse effects (Allahabi *et al.,* 2022). In a study conducted on animals, the traditional Ayurvedic formulation known as "Tryushanadya Lauha" demonstrated promising results as a hypoglycaemic formulation (Swer *et al.,* 2023). There is a clear shift in the global trend of using natural medicines instead of chemical ones. The medicinal properties of plants are highly appreciated around the globe and have been recognized since ancient times as an abundant supply of therapeutic compounds for avoiding the development of illnesses and afflictions (Ashraf *et al.,* 2024). Still, we have to go a long way to find an effective and safe drug for the management of the diabetes.

This study aimed to assess the hypoglycemic effect of HMF in diabetic rats caused by streptozotocin and nicotinamide. The STZ-Nic. model was used because of the fact that it creates a model which represent diabetes mellitus type 2 with mild hyperglycaemia. The results showed that following a 14 day course of treatment, BG levels decreased in both the standard control and HMF groups. In comparison to the STZ-Nic. Control group, the fasting glucose levels of the glibenclamide, HMF-700, and HMF-1400 mg/kg treatment groups significantly decreased on day 28. According to the current research, HMF 1400 mg/kg was successful in causing a discernible drop in the BG level in diabetic STZ-Nic. rats.

The HMF formulation is composed of 12 ingredients, Tabasheer is first ingredient that possess secondary metabolites, like stigmasterol and β-sitosterol glucoside. According to a study, leaf extract of *B. bambos* may be advantageous in the management of hyperglycaemia (Nazreen *et al.,* 2011). Liquorice has ability to reduce disaccharide degradation from reducing α-glucosidase and á-amylase function of enzymes, which improves BG management among people with diabetes and lowers the risk of hyperglycaemia following meals (Sharma *et al.,* 2017). *Rumex vesicarius* has flavonoid called luteolin; it has a great potential to reduce BG level. It may interact with the enzyme α-glucosidase, resulting in powerful antidiabetic effects (Al-Masri *et al.,* 2023).

Coriander seed contains polyphenolic compounds, which have antioxidant and antiinflammatory properties. These properties are directly proportional to antidiabetic activity (Scandar *et al.,* 2023). Lactucaxanthin, a carotenoid derived from *L. sativa*, significantly reduced hyperglycemia in STZ-Nic induced diabetic rats by inhibiting the enzymes α-glucosidase and amylase (Gopal *et al.,* 2017). Purslane has shown strong antioxidant activity which in turn may act as antidiabetic and it can reduce the BG level (Hu *et al.,* 2019). Sandal wood has ability to reduce cholesterol level; may be for this reason it can stop insulin resistance from developing, improve glycaemic control by preserving insulin levels, and stop more beta cell damage (Kulkarni *et al.,* 2012).

Gulnar can also decrease the hyperglycaemia. Its methanolic extract has gallic acid and it reduces the hyperglycemic condition (Chattopadhyay *et al.,* 2022). The hypoglycaemic action of *A. nilotica* results from the its direct or indirect stimulation of the β-cells in islets of langerhans, to release more insulin (Roozbeh *et al.,* 2017). *C. camphora* and *C. sativum* L. have been shown to reduce inflammation by lowering TNF-α, IL-6, and MDA levels all of which are high in diabetes caused by STZ and to improve antioxidant status by raising superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH). The bioactive component cyanidin of *C. camphora* was shown to inhibit α-glucosidase (Laribi *et al.,* 2015).

HMF underwent the process of pesticide contamination test, using the certified test method R-44. All of the pesticides remained within permissible limits. This implies that the research specimen is pesticide-free and is secure to consume. In organoleptic test, Alkaloids, flavonoids, phenols, proteins, tannins, steroids, starch were all detected in the sample according to preliminary phytochemical analyses of HMF. Hence, it can be said that the antihyperglycaemia action of HMF in rats is perhaps partially due to the positive effects of the bioactive constituents.

5. Conclusion

The primary goal of this research study was to assess the hypoglycaemic effects of an Unani HMF in STZ-Nic. induced diabetic rats. The safety of the HMF was assessed by biochemical indicators of liver and kidney functions. The OGTT and STZ-Nic. induced diabetes mellitus model was used to check the efficacy of the study formulation.

According to the results of the OGTT test, rats treated with glibenclamide and HMF 1400 mg/kg had significantly lower BG levels at 60 min, while at 120 min, only rats treated with glibenclamide showed the similar tendency. It suggests that the HMF in dose of 1400 mg/kg was effective in lowering the BG after 60 min. The test formulation HMF at dose of 700 mg/kg and 1400 mg/kg had lowered the FBG after 14 days of treatment but the results were not significant when compared to glibenclamide treatment. The formulation at both dose levels had lowered the FBG after 28 days of treatment. The body weight of the diabetic rats decreased during the treatment and neither glibenclamide nor HMF at both dose levels increased body weight significantly as compared to vehicle control. The standardization of the test formulation was done by organoleptic features and HPTLC fingerprinting along with the estimation of heavy metal, pesticide, aflatoxin and microbial load for placing fingerprinting of the formulation. The results showed that Unani HMF is effective and safe therapy for diabetes mellitus. The limitation of this study includes lack of toxicity study and in future it may be planned and executed followed by clinical trial.

Acknowledgments

The authors express gratitude to the Director General of CCRUM, New Delhi, for the support and resources provided for this research.

Conflicts of interest

The authors declare no conflicts of interest relevant to this article.

References

Akram, S.A.W.; Arokiarajan, M.S.; Christopher, J.J.; Jameel, M.; Saquib, M.; Saripally, T.S.K.; Anwar, N.; Asif, M. and Ahmed K.K. (2024). Antimicrobial and antioxidant study of combined essential oils of *Anethum sowa* Kurz., and *Trachyspermum ammi* (L.) along with quality determination, comparative histoanatomical features, GC-MS and HPTLC chemometrics. Sci. Rep., **14**:27010, https://doi.org/10.1038/s41598-024-75773-8.

Allahabi, Z. and Singh, S. (2022). *In silico* approach for discovery of drug against the peroxisome proliferator-activated receptor gamma for diabetes treatment. Ann. Phytomed., **11**(1):299-310.

Al-Masri, A.A.; Ameen, F.; Davella, R. and Mamidala, E. (2023). Antidiabetic effect of flavonoid from *Rumex vesicarius* on alloxan induced diabetes in male albino wistar rats and its validation through *in silico* molecular docking and dynamic simulation studies. Biotech. Genetic Engin. Rev., **40**(4):4479-4494, https://doi.org/10.1080/02648725.2023.2213042.

Anwar, K.R.; Badruddeen, A.J.; Khan, M.I. and Ahmad, M. (2024). An outlook on pathological pathways of diabetes and molecular mechanisms of antidiabetic phytobioactives. Letters in Functional Foods, **1**(1):e180723218858, https://doi:10.2174/266693 90016662 30718142652.

Ashraf, N.; Naikodi, M.A.R.; Kumar, G.S.; Ahmed, T.; Munshi Y.I. and Zakir, M. (2024). Physicochemical standardization, evaluation of antioxidant and antimicrobial activity of a polyherbal formulation. Ann. Phytomed., **13**(2):726-733, http://dx.doi.org/10.54085/ap.2024.13.2.74.

Chan, J.C.; Malik, V.; Jia, W.; Kadowaki, T.; Yajnik, C.S.; Yoon, K.H. and Hu, F.B. (2009). Diabetes in Asia: Epidemiology, risk factors, and pathophysiology. JAMA, **301**(20):2129-2140, https://doi:10.1001/jama.2009.726.

Chattopadhyay, K.; Wang, H.; Kaur, J.; Nalbant, G.; Almaqhawi, A.; Kundakci, B.; Panniyammakal, J.; Heinrich, M.; Lewis, S.A.; Greenfield, S.M.; Tandon, N.; Biswas, T.K.; Kinra, S. and Leonardi-Bee, J. (2022). Effectiveness and safety of Ayurvedic medicines in type 2 diabetes mellitus management: A systematic review and meta-analysis. Front. Pharmacol., **13**:821810, https://doi.org/10.3389/fphar.2022.821810.

Christopher, J.J.; Akram, S.A.W.; Arokiarajan, M.S.; Jameel, M.; Saripalli, T.S.K.; Ahmed, V.M.; Anwar, N. and Ahmad, K.K. (2024). The qualitative and histoanatomical validation of *Daucus carota* L., fruit along with in vitro cytotoxic, antioxidants and antimicrobial analysis. Food and Humanity, **3**:100326, https://doi.org/10.1016/j.foohum. 2024.100326.

Dwivedi, D.K. and Jena, G.B. (2023). Dimethyl fumarate-mediated Nrf2/ARE pathway activation and glibenclamide-mediated NLRP3 inflamma some cascade inhibition alleviate type II diabetes-associated fatty liver in rats by mitigating oxidative stress and inflammation. J. Biochem. Mol. Toxicol., **37**(7):e23357, doi:10.1002/jbt.23357.

Eshan, B.S.; Shetty, A.; Shetgaonkar, N. and Fernandes, Z. (2023). Antidiabetic potential of *Bunchosia glandulifera* (Jacq.) Kunth leaf extract in diabetic rats: *In vivo, in vitro* and *in silico* analysis. Ann. Phytomed., **12**(2):555-561.

Fowler, M.J. (2008). Microvascular and macrovascular complications of diabetes. Clin. Diabetes, **26**(2):77-82, https://doi.org/10.2337/diaclin.26.2.77.

Gopal, S.S.; Lakshmi, M.J.; Sharavana, G.; Sathaiah, G.; Sreerama, Y.N. and Baskaran, V. (2017). Lactucaxanthin a potential antidiabetic carotenoid from lettuce (*Lactuca sativa*) inhibits α-amylase and α-glucosidase activity *in vitro* and in diabetic rats. Food and function, **8**(3):1124-31, https://doi.org/10.1039/C6FO01655C.

Hashim, M.; Badruddeen, U.; Akhtar, J.; Khan, M.I.; Ahmad, M.; Islam, A. and Ahmad, A. (2024). Diabetic neuropathy: An overview of molecular pathways and protective mechanisms of phytobioactives. Endocr. Metab. Immune Disord. Drug Targets, **24**(7):758-776, https://doi:0.2174/0118715303266444231008143430.

Hossain, M.J.; Al-Mamun, M. and Islam, M.R. (2024). Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health Sci. Rep., **7**(3):e2004, doi:10.1002/hsr2.2004.

Hu, Q.; Niu, Q.; Song, H.; Wei, S.; Wang, S.; Yao, L. and Li, Y.P. (2019). Polysaccharides from *Portulaca oleracea* L. regulated insulin secretion in INS-1 cells through voltage-gated Na+ channel. Biomed. Pharmacother., **109**:876-885, https://doi.org/10.1016/j.biopha. 2018.10.113.

Husain, G.M.; Singh, P.N. and Kumar, V. (2009). Beneficial effects of a standardized *Hypericum perforatum* extract in rats with experimentally induced hyperglycemia. Drug Discov. Ther., **3**(5):215-220.

IDF (International Diabetes Federation). (2025). IDF Diabetes Atlas, 11th edition, ISBN: 978-2-930229-96-6, available from, https://www.diabetesatlas.org.

Karamanou, M.; Protogerou, A.; Tsoucalas, G.; Androutsos, G. and Poulakou-Rebelakou, E. (2016). Milestones in the history of diabetes mellitus: The main contributors. World J. Diabetes, **7**(1):1-7, https://doi:10.4239/wjd.v7.i1.1.

Khan, D.H. (1944). Risala Ziabitus, special edition of Al-Shifa, Delhi, pp:51.

Kulkarni, C.R.; Joglekar, M.M.; Patil, S.B. and Arvindekar, A.U. (2012). Antihyperglycemic and antihyperlipidemic effect of *Santalum album* in streptozotocin induced diabetic rats. Pharm. Biol., **50**(3):360-365, https://doi.org/10.3109/13880209.2011.604677.

Laribi, B.; Kouki, K.; M'Hamdi, M. and Bettaieb, T. (2015). Coriander (*Coriandrum sativum* L.) and its bioactive constituents, Fitoterapia, **103**:9-26, https://doi.org/10.1016/j.fitote.2015.03.012.

Majusi, A. (2010). Kamil-us-Sanat (Urdu translation), Vol-2, Part-2, CCRUM, Ministry of Health and Family Welfare, Govt. of India, New Delhi, pp:192.

Masiello, P.; Broca, C.; Gross, R.; Roye, M.; Manteghetti, M.; Hillaire-Buys, D.; Novelli, M. and Ribes, G. (1998). Experimental NIDDM: Development of a new model in adult rats administered streptozotocin and nicotinamide. Diabetes, 47(2):224-229, https://doi.org/10.2337/diab.47.2.224.

Nabrdalik, K.; Skonieczna-¯ydecka, K.; Irlik, K.; Hendel, M.; Kwiendacz, H.; £oniewski, I.; Januszkiewicz, K.; Gumprecht, J. and Lip, G.Y. (2022). Gastrointestinal adverse events of metformin treatment in patients with type 2 diabetes mellitus: A systematic review, meta-analysis and meta-regression of randomized controlled trials. Front. Endocrinol., 13:912-975, https://doi.org/10.3389/fendo.2022.975912.

Nazreen, S.; Kaur, G.; Alam, M.M.; Haider, S.; Hamid, H. and Alam, M.S. (2011). Hypoglycemic activity of *Bambusa arundinacea* leaf ethanolic extract in streptozotocin induced diabetic rats. Pharmacologyonline, 1:964-72.

NFUM, National Formulary of Unani Medicine, (2007). Part-II, Vol. I. CCRUM, Dept. of AYUSH, Ministry of Health and Family Welfare, Govt. of India; New Delhi. pp:177-190

Petersmann, A.; Müller-Wieland, D.; Müller, U.A.; Landgraf, R.; Nauck, M.; Freckmann, G.; Heinemann, L. and Schleicher, E. (2019). Definition, classification and diagnosis of diabetes mellitus. Exp. Clin. Endocrinol. Diabetes, 127(S01):S1-S7, https://doi:10.1055/a-1018-9078.

Pfeiffer, A.F. and Klein, H.H. (2014). The treatment of type 2 diabetes. Dtsch. Arztebl. Int., 111(5):69-81, doi:10.3238/arztebl.2014.0069.

Qurshi, A.A. (2022). Moalajat Nafeesi (Urdu translation), Idara Kitabus Shifa, New Delhi, pp:805.

Rayner, C.K.; Samsom, M.; Jones, K.L. and Horowitz M. (2001). Relationships of upper gastrointestinal motor and sensory function with glycemic control. Diabetes Care, 24(2):371-381, https://doi.org/10.2337/diacare.24.2.371.

Reagan Shaw, S.; Nihal, M. and Ahmad, N. (2008). Dose translation from animal to human studies revisited. FASEB J., 22(3):659-661, https://doi.org/10.1096/fj.07-9574LSF.

Roozbeh, N.; Darvish, L. and Abdi, F. (2017). Hypoglycemic effects of *Acacia nilotica* in type II diabetes: A research proposal. BMC Res. Notes, 10(331):1-5, https://doi.org/10.1186/s13104-017-2646-1.

Scandar, S.; Zadra, C. and Marcotullio, M.C. (2023). Coriander (*Coriandrum sativum*) polyphenols and their nutraceutical value against obesity and metabolic syndrome. Molecules, 28(10):4187, https://doi.org/10.3390/molecules 28104187.

Sharma, V.; Katiyar, A. and Agrawal, R.C. (2017). *Glycyrrhiza glabra*: Chemistry and pharmacological activity. Sweeteners, 31:87-100, doi:10.1007/978-3-319-27027-2_21.

Shaw, J.E.; Sicree, R.A. and Zimmet, P.Z. (2010). Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res. Clin. Pract., 87(1):4-14, https://doi.org/10.1016/j.diabres.2009.10.007.

Sina, I. (2010). Al Qanoon Fit Tib, Vol-4, Idara Kitabus Shifa, New Delhi, pp:1031-1032.

Swer, H.; Kandalkar, U.; Katore, A.; Tajane, Y. and Wanjari, A. (2023). Assessment of comparative antidiabetic activity of herbomineral formulations (Tryushanadya lauha and Tryushanadya mandur) in wistar rats. Ann. Phytomed., 12(2):545-554.

Szkudelski, T. (2012). Streptozotocin nicotinamide induced diabetes in the rat. Characteristics of the experimental model. Exp. Biol. Med., 237(5):481-490, https://doi:10.1258/ebm.2012.011372.

Zimmet, P.; Alberti, K. and Shaw, J. (2001). Global and societal implications of the diabetes epidemic. Nature, 414:782-787, https://doi.org/10.1038/414782a.

Citation **Khan Asma Mohd Anis, Vellanki Manvitha, Gulam Mohammed Husain, Durgesh Kumar Dwivedi, Tirumala Santhoshkumar Saripalli, Younis Iftikhar Munshi and Mohammad Zakir (2025). Evaluation of antidiabetic activity of an Unani herbomineral formulation in nicotinamide streptozotocin induced diabetic rats. Ann. Phytomed., 14(1):608-621. http://dx.doi.org/10.54085/ap.2025.14.1.58.**