Antidiabetic, Hypolipidemic, Hepatoprotective, and Hematological effects of the aqueous extract of *Balanites aegyptiaca* fruit-mesocarp in Alloxan-induced Diabetic Wistar rats

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Abstract
Diabetes mellitus is a chronic metabolic disorder often accompanied by secondary biochemical and hematological complications. *Balanites aegyptiaca* (Desert Date) is traditionally used to manage diabetes, but a comprehensive assessment of its therapeutic efficacy and systemic safety profile remains essential. This study evaluated the antidiabetic, hypolipidemic, hepatoprotective, and hematological effects of the aqueous extract of *Balanites aegyptiaca* fruit-mesocarp in alloxan-induced diabetic Wistar rats. Twenty-five Wistar rats were divided into five groups: normal control, diabetic untreated control, diabetic treated with metformin (50 mg/kg bw), and two diabetic groups treated with the extract at doses of 200 mg/kg bw and 400 mg/kg bw, respectively, over a 28-day period. Fasting blood sugar (FBS), liver function biomarkers, lipid profiles, and hematological parameters were determined. Oral administration of the extract at both 200 mg/kg and 400 mg/kg significantly ($p < 0.05$) reduced FBS from day 14 onwards, achieving glycemic control (3.63 mmol/L and 3.97 mmol/L, respectively, by day 28) comparable to metformin (3.60 mmol/L). In the lipid profile, the 400 mg/kg dose optimized lipid metabolism by increasing high-density lipoprotein (HDL) and keeping low-density lipoprotein (LDL) minimal. Hematologically, the extract significantly reduced elevated white blood cell counts ($p < 0.05$) seen in diabetic rats, while the 400 mg/kg dose significantly increased red blood cell counts ($p < 0.05$) compared to all other groups. However, extract administration resulted in a significant elevation of alanine aminotransferase (ALT) levels ($p < 0.05$), implying potential mild hepatic strain at higher doses despite stable alkaline phosphatase (ALP) activity. The aqueous extract of *Balanites aegyptiaca* fruit-mesocarp possesses potent hypoglycemic, hypolipidemic, and erythropoietic properties, validating its ethnomedicinal use. However, the observed elevation in ALT warrants cautious dosage management regarding potential hepatic monitoring in long-term applications.

Keywords: *Balanites aegyptiaca*, Alloxan, Hypoglycemic, Lipid Profile, Hepatotoxicity, Wistar Rats.

INTRODUCTION
Diabetes mellitus represents one of the most pervasive, accelerating, and challenging chronic metabolic disorders globally, characterized by persistent fasting hyperglycemia resulting from defects in insulin secretion, peripheral insulin action, or both (Odeniran, 2025). The chronic elevation of circulating blood glucose triggers systemic oxidative stress, leading to a cascade of profound secondary physiological complications (Abou Khalil, 2016). Among these, diabetic dyslipidemia which is marked by abnormal shifts in systemic lipid fractions has been shown to accelerate cardiovascular risk, while simultaneous alterations in hematological profiles often compromise systemic immunity and oxygen-carrying capacity (Ezzat, 2026). Furthermore, the

liver, as a central hub for glucose and lipid homeostasis, frequently suffers tissue microdamage during uncontrolled diabetes, resulting in the leakage of intracellular enzymes into the bloodstream (Gamde *et al.,* 2023). In experimental biomedical research, alloxan monohydrate is widely utilized to simulate this disease state due to its ability to selectively destroy insulin-producing pancreatic beta cells via reactive oxygen species generation, effectively mimicking the clinical manifestations of insulin-dependent diabetes (Odeniran, 2025).

To mitigate these widespread systemic complications, conventional oral hypoglycemic therapies, such as the biguanide metformin, are universally prescribed. Metformin primarily works by activating adenosine monophosphate-activated protein kinase (AMPK), thereby suppressing hepatic gluconeogenesis and increasing peripheral insulin sensitivity (Zaky *et al.,* 2022). However, the high economic cost, limited rural accessibility, and adverse side effects associated with synthetic agents ranging from persistent gastrointestinal distress to rare instances of lactic acidosis have driven intensive global research into exploring safer, cost-effective, bioactive alternatives derived from ethnomedicinal plants (Abou Khalil, 2016; Murthy *et al.,* 2021).

Balanites aegyptiaca (L.) Delile, popularly termed the "Desert Date" and belonging to the Zygophyllaceae family, is a resilient multi-purpose tree native to the arid and semi-arid regions of Africa and South Asia (Murthy *et al.,* 2021). In various regional systems of traditional medicine, distinct parts of the plant are deployed to manage diverse ailments, with the fruit-mesocarp specifically favored as a traditional oral therapy for diabetes mellitus (El Deib, 2020; Kamel *et al.,* 1991). Phytochemical investigations reveal that the *Balanites aegyptiaca* fruit pulp is an exceptionally rich source of specialized secondary metabolites, including steroidal saponins, flavonoids, organic acids, and coumarins (Murthy *et al.,* 2021; Turaki *et al.,* 2025). These bioactive compounds have been shown to stimulate endogenous insulin secretion, upregulate glucose transporter expressions (such as GLUT-2 and GLUT-4), and inhibit intestinal alpha-amylase activity to modulate glucose absorption (El Deib, 2020; Zaky *et al.,* 2022).

While preliminary studies confirm the basic hypoglycemic efficacy of *Balanites aegyptiaca* (Kamel *et al.,* 1991), a critical requirement exists to rigorously establish its broader physiological impacts and systemic safety profile across a unified experimental model. It is well understood that herbal extracts containing potent saponins can exert dual effects, acting therapeutically on metabolic pathways while concurrently presenting risk profiles for mild cellular toxicity in clearance organs like the liver (Murthy *et al.,* 2021; Gamde *et al.,* 2023). Therefore, mapping how its aqueous fruit extract alters hepatic function biomarkers, circulating lipid fractions, and hematological health alongside its primary glycemic control is essential to delineate its therapeutic index. Therefore, the aim of this study was to evaluate the antidiabetic, hypolipidemic, and hematoprotective properties of *Balanites aegyptiaca* fruit-mesocarp aqueous extract in alloxan-induced diabetic rats

METHODS

Sample Collection

The fruits of *Balanites aegyptiaca* were harvested from Kalgo Farm, located within the Kalgo Local Government Area of Kebbi State, Nigeria. Taxonomic authentication of the plant material was performed by an expert taxonomist in the Department of Biological Sciences at the Federal University Birnin Kebbi, where a voucher specimen was assigned the reference number FUBK/HERB/0321 and deposited in the institutional herbarium. For extract preparation, the fruits were thoroughly washed with distilled water, and the pulp (mesocarp) was manually separated, cleaned, and subjected to shade-drying to preserve thermolabile constituents. The desiccated mesocarp samples were subsequently macerated by soaking in distilled water for 72 hours, with

intermittent agitation to maximize solute extraction. Following the maceration period, the mixture was filtered through muslin cloth. The resulting filtrate was concentrated to dryness under reduced pressure using a rotary evaporator maintained at 60 °C. The dried crude aqueous extract was transferred into an airtight container and stored in a refrigerator at -4 °C for subsequent experimental applications.

Experimental Animals and Induction of Diabetes

Experimental Animals and Ethical Approval

Adult male Wistar rats (100 – 200g) were procured from Sokoto, Nigeria, and housed in secure iron cages. The animals were maintained on a standard commercial pellet diet with *ad libitum* access to water throughout the study. Prior to the commencement of the experimental procedures, the rats were allowed to acclimatize to the laboratory environment for a period of 7 days. All experimental protocols were approved by the Federal University Research Ethics Committee (Approval No: FUBK/ETH/034).

Induction of Diabetes and Treatment Protocol

Baseline blood glucose levels were determined for all animals prior to the induction of diabetes. Following a 12-hour fast, a single dose of alloxan (160 mg/kg body weight) was administered intraperitoneally. To prevent initial drug-induced hypoglycemic shock, the animals were supplied with a 20 % glucose solution 6 hours post-induction, in accordance with the protocol described by Stanley *et al.* (2001).

Hyperglycemia was confirmed 72 hours after alloxan administration; rats presenting with sustained blood glucose levels exceeding 7 mmol/L were selected for the study. The experimental groups were subsequently treated with the extract once daily for a duration of 28 days.

Experimental Design

The study utilized a total of 25 Wistar rats, which included 20 surviving diabetic models and 5 non-diabetic controls (Table 1). Both the plant extract and the reference drug were administered daily via oral gavage using a gastric cannula for a total duration of 28 days. Upon completion of the 28-day treatment period, the animals were humanely euthanized via chloroform inhalation. Blood samples were immediately harvested via cardiac puncture and collected into plain and anticoagulant-coated tubes. To obtain serum for downstream biochemical assays, the whole blood samples were centrifuged at 5000 rpm for 5 minutes.

Table 1: Experimental Design

GROUP	TREATMENT
1	Normal Wistar Rats given only feed and water
2	Untreated Alloxan-induced diabetic Wistar Rats
3	Alloxan-induced diabetic Wistar Rats treated with metformin at 50mg/kg body weight
4	Alloxan-induced diabetic Wistar Rats treated with *Balanites aegyptiaca* extract at 200mg/kg body weight
5	Alloxan-induced diabetic Wistar Rats treated with *Balanites aegyptiaca* extract at 400mg/kg body weight

Biochemical Assays

Blood Glucose

Determination of blood glucose was executed using the standard glucose oxidase methodology outlined by Siraj *et al*. (2025). The underlying principle involves the oxidation of glucose to gluconic acid and hydrogen peroxide via glucose oxidase, with the latter product reacting with 4-aminoantipyrine under peroxidase catalysis to generate a pink quinoneimine chromophore. Operationally, plasma was combined with the reactive enzyme cocktail and subjected to a 10-minute incubation period at 37°C. Following this, absorbance values were acquired at 500 nm relative to a reagent blank, and sample glucose values were derived from a known standard curve.

Serum Proteins

The concentration of total serum protein was quantified colorimetrically using the Biuret reaction, in which peptide bonds in serum proteins interacted with cupric ions in an alkaline environment to produce a distinctive blue coordination complex, with intensity directly correlating to protein concentration (Andarge and Megerssa, 2024). The experiment was conducted by making three separate reaction tubes labelled as blank, standard, and sample. A 1000 µL aliquot of the Biuret reagent was added to each of the three tubes, followed by the addition of 20 µL of the standard solution and 20 µL of the serum sample to their corresponding tubes. The contents of each tube were meticulously combined and incubated for 10 minutes at 35°C to facilitate perfect colour development. Subsequent to incubation, the spectrophotometric absorbances of both the standard and the test sample were assessed against the reagent blank to determine the final total protein concentration.

Albumin

Serum albumin concentration was determined based on the principle that the binding of albumin to a bromocresol green (BCG) solution induces a proportional colorimetric shift, with Brij 35 incorporated into the reagent matrix to prevent turbidity and improve assay linearity (Andarge and Megerssa, 2024)). Operationally, the procedure was carried out by dispensing 4 mL of the working BCG reagent into three distinct tubes designated as test, standard, and blank. Subsequently, 0.02 mL of the serum sample was added to the test tube, and 0.02 mL of the standard solution was introduced into the standard tube. The contents of the tubes were thoroughly mixed and allowed

to stand at room temperature for 10 minutes to ensure stable color development. Following this incubation period, the spectrophotometric absorbance of the test and standard mixtures were read at 620 nm after zeroing the instrument against the reagent blank.

Lipid Profile

Component lipid fractions were quantified using commercial enzymatic colorimetric diagnostic kits obtained from Randox Laboratories (Antrim, UK). Serum triglycerides were determined via the GPO-PAP method, total cholesterol (TC) was estimated using the CHOD-PAP and high-density lipoprotein cholesterol (HDL) as described by Siraj *et al.* (2025). The experimental procedures for TC, triglycerides, and HDL were carried out using three distinct test tubes marked as blank (B), standard (S), and test (T). For total cholesterol determination, 2.0 mL of color reagent was dispensed into all tubes, which was then combined with 0.2 mL of distilled water in the blank, 0.2 mL of cholesterol standard in the standard tube, and 0.02 mL of serum in the test tube, followed by incubation at 37°C for 10 minutes. The serum triglyceride assay followed an identical pipetting scheme, substituting the standard with 0.2 mL of triglyceride standard and incubating the reaction mixture at 37°C for 10 minutes (or at 25°C for 30 minutes). Similarly, HDL was quantified by mixing 2.0 mL of cholesterol reagent with 0.2 mL of distilled water (blank), 0.2 mL of standard supernatant (standard), and 0.02 mL of sample supernatant (test), followed by a matching incubation phase where the resulting color intensity remained stable for 30 minutes. Following spectrophotometric measurement, very low-density lipoprotein cholesterol (VLDL-c) content was calculated by dividing the serum triglyceride concentration by a factor of 5, a constant predicated on the fixed 1:5 ratio of VLDL to total plasma triglycerides in fasting subjects with triglyceride levels below 400 mg/dL. Finally, low-density lipoprotein cholesterol (LDL-c) concentrations were estimated by subtracting the sum of HDL-c and VLDL-c from the total cholesterol value using the Friedewald equation (Warnick *et al.*, 1990).

Liver Function Enzymes

Alanine Aminotransferase (ALT) Activity.

The technique developed by Reitman and Frankel (1957) and as reported by Shemishere *et al.* (2026) was employed to assess ALT activity. ALT catalyses the conversion of alanine and 2-ketoglutarate into pyruvate and glutamate; pyruvate then interacts with 2, 4-dinitrophenylhydrazine (DNPH) to yield a red-brown hydrazone at 546 nm.

The test tube bottles with the proper labels were filled with 0.1 mL of serum. Subsequently, 1 mL of the working reagent was added to each test tube, which was then mixed and incubated for 1 minute at 37 °C.

The absorbance was measured at 546 nm. The activity was determined as follows:
ALT activity (U/L) = (ΔOD/min) x 1745

Aspartate Aminotransferase (AST) Activity.

AST activity techniques of Reitman and Frankel (1957) and reported by Shemishere *et al.* (2026) was used. Aspartate aminotransferase (AST), also known as glutamate oxaloacetate transaminase (GOT), is the enzyme that facilitates the transamination of aspartate and 2-oxaloacetate to generate oxaloacetate, which then interacts with 2,4-dinitrophenyl hydrazine to yield hydrazine (Reitman and Frankel, 1957). The test tube vials were lined with corresponding labels and the sample was dispensed into each one (0.1 mL). Subsequently, 1 mL of working reagent was added to each test tubes, which were then mixed completely and incubated for 1 minute at 37°C. The absorbance was measured at 546 nm. The computation of activity was: AST activity (U/L) = (ΔOD/min) x 1745

Activity of Alkaline Phosphatase (ALP)

The activity of ALP was evaluated according to Ghosh and Roy (2014). At pH 10.5, p-nitrophenylphosphate was hydrolysed by alkaline phosphatase to p-nitrophenol, which was quantified at 405 nm. After transferring 0.5 mL of the process to one test tube, 0.05 mL of the control, standard, and sample were added to their appropriate tubes, along with alkaline phosphatase substrate. The mixture was incubated at 37 °C, during which 2.5 mL of alkaline phosphatase colour developer was added at specified intervals. The test tube was mixed, and the absorbance was initially measured against a blank at 590 nm after 1, 2, and 3 minutes.

$$\text{ALP activity (U/L)} = \frac{Absorbance\ of\ unknown}{Absorbance\ of\ standard} \times \text{value of standard}$$

Haematological Parameters

Hematological analysis was performed as described by Isah *et al.* (2017) to evaluate key parameters, including white blood cell count (WBC), hemoglobin concentration (HGB), red blood cell count (RBC), hematocrit/packed cell volume (HCT/PCV), and mean corpuscular volume (MCV).

Statistical Analysis

Results were presented as mean ± standard deviation (SD). Where applicable, the results were subjected to further statistical analysis using One-Way Analysis of Variance (ANOVA) followed by the Duncan's post hoc test. (p<0.05) were considered significant.

Results

Effects of *Balanites aegyptiaca* Extract on Fasting Blood Sugar (FBS) and Weight Changes

As shown in Table 2, The administration of alloxan successfully induced severe hyperglycemia in Wistar rats, as evidenced by a substantial increase in fasting blood sugar (FBS) in Group 2 (untreated diabetic control) compared to Group 1 (normal control) from Day 1 through Day 28 (p < 0.05). Oral administration of *B. aegyptiaca* fruit-mesocarp aqueous extract elicited a potent, time-dependent antidiabetic effect. By Day 7, both the 200 mg/kg body weight (Group 4) and 400 mg/kg) (Group 5) extract-treated groups demonstrated significant reductions in FBS compared to the untreated diabetic group (p < 0.05). By Day 14 and Day 28, the FBS levels of both extract-treated groups had normalized completely, showing no statistically significant difference (p > 0.05) when compared to either the normal control (Group 1) or the standard drug metformin (Group 3).

Alloxan-induced diabetes mellitus was characterized by a progressive and severe loss of body weight in the untreated diabetic group (Group 2) over the 28-day experimental period. This significant wasting of structural proteins and muscle mass is a hallmark of uncontrolled hyperglycemia, where the body is unable to utilize glucose for energy. Conversely, oral administration of the aqueous extract of *Balanites aegyptiaca* fruit-mesocarp effectively reversed this weight loss. Both the 200 mg/kg (Group 4) and 400 mg/kg (Group 5) extract-treated groups demonstrated a progressive stabilization and subsequent gain in body weight, behaving in a manner statistically comparable (p > 0.05) to the standard drug metformin (Group 3). By Day 28,

the extract-treated animals showed healthy weight recovery profiles, signifying an improvement in metabolic efficiency and a reversal of diabetic cachexia.

Table 2: Effects of Administration of Aqueous Extracts of *Balanites aegyptiaca* Fruit-Mesocarp on Fasting Blood Sugar in Alloxan-induced Diabetic Wistar Rats.

GROUP	DAY 1 (mmol/L)	DAY 7 (mmol/L)	DAY 14 (mmol/L)	DAY 28 (mmol/L)
1	5.74± 1.30 ^{b}	5.17 ± 1.61^{b}	5.15± 0.79^{b}	4.95 ± 0.68^{b}
2	18.43± 2.83 ^{a,c}	18.07 ± 4.29^{a,c}	22.47± 5.43^{a}	19.60 ± 5.47^{a}
3	8.70± 1.61^{b}	5.17 ± 0.59^{b}	3.77± 0.31^{b}	3.60 ± 0.17^{b}
4	17.13± 2.51^{a,c}	10.23 ± 0.67^{b,c}	5.03± 0.68^{b}	3.63 ± 0.25^{b}
5	20.33± 2.31^{a}	9.83 ± 1.15^{b,c}	5.50± 1.05^{b}	3.97 ± 0.57^{b}

Results are presented in Mean ± SEM (n = 5). Values with superscript a, b, and c means a significant difference when compared to group 1, 2 and 3 respectively ($p < 0.05$).

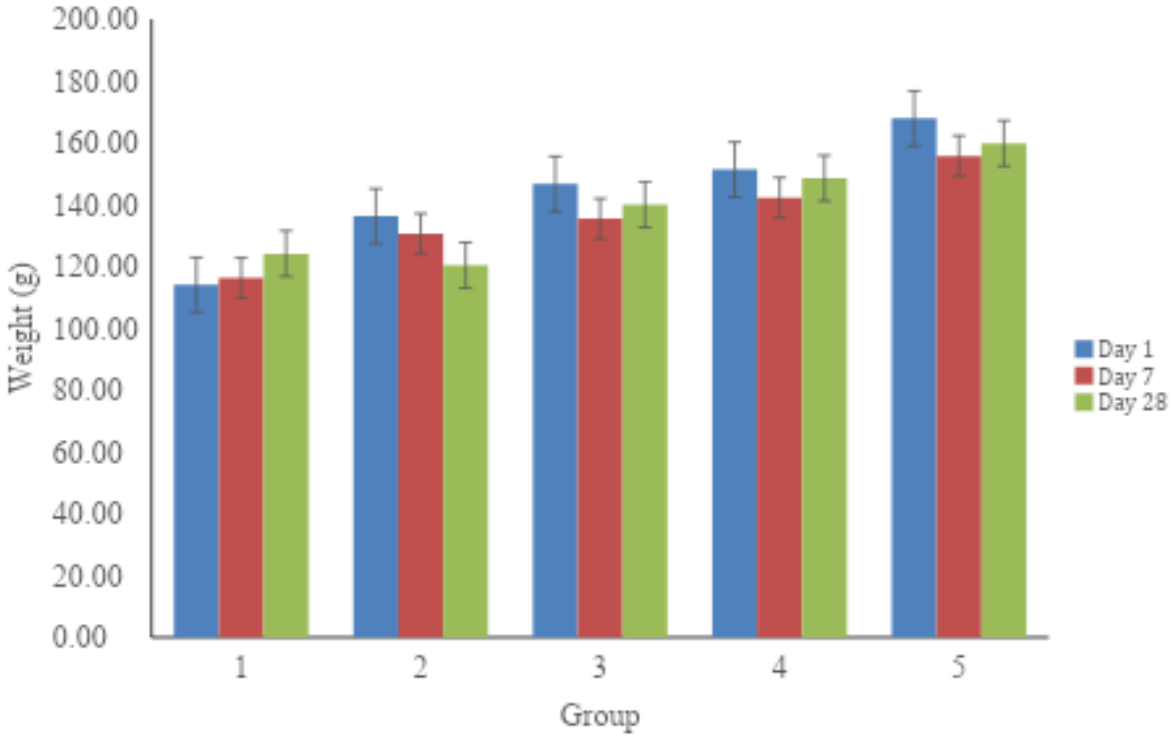

Figure 1: Effects of Oral Administration of Aqueous Extract of *Balanites aegyptiaca* Fruit-Mesocarp on Body Weight in Alloxan-induced Diabetic Wistar Rats.

Effect on Lipid Profiles

The lipid profiles across the groups exhibited notable variations following treatment (Table 3). Group 4 (200mg/kg extract) displayed elevated total cholesterol, triglycerides and LDL cholesterol. Conversely, the higher dose of the extract (400 mg/kg, Group 5) demonstrated a favorable hypolipidemic profile. In Group 5, total cholesterol, and LDL were suppressed, while high-density lipoprotein (HDL) cholesterol was maximized outperforming all other experimental groups including the normal and metformin controls.

Table 3: Effect Oral Administration of Aqueous Extract of *Balanites aegyptiaca* Fruit-Mesocarp on Lipid profile of diabetic induced Wistar rats

Group	TOTAL CHOLESTEROL (mg/dL)	TRIGLYCERIDE (mg/dL)	HDL (mg/dL)	LDL (mg/dL)
1	1.57 ± 0.33	0.57 ± 0.04	0.88 ± 0.01	0.43 ± 0.05
2	1.38 ± 0.13	0.45 ± 0.01	0.74 ± 0.02	0.43± 0.06
3	1.25 ± 0.16	0.60 ± 0.02	0.65 ± 0.03	0.32 ± 0.01
4	1.82 ± 0.11	0.88 ± 0.03	0.74 ± 0.06	0.67 ± 0.03
5	1.49 ± 0.06	0.40 ± 0.03	0.93 ± 0.05	0.38 ± 0.07

Effect on Liver Function Biomarkers

Alloxan-induced diabetes was associated with alterations in hepatic biomarkers (Table 4). Serum alkaline phosphatase (ALP) activity was significantly elevated in the untreated diabetic group relative to the normal control ($p < 0.05$). Treatment with the 400 mg/kg extract significantly restored ALP activity back to baseline baseline levels ($p < 0.05$). However, serum alanine aminotransferase (ALT) activity was unexpectedly higher in the extract-treated groups (Groups 4 and 5) compared to both the normal and diabetic controls ($p < 0.05$), while aspartate aminotransferase (AST) activity remained statistically unaltered across all experimental groups ($p > 0.05$). Total protein and albumin profiles revealed notable changes; total protein increased significantly in the untreated diabetic group compared to the normal control and was further elevated in the metformin and 400 mg/kg extract groups ($p < 0.05$). Serum albumin levels showed a significant increase exclusively in the extract-treated groups compared to the normal and diabetic controls ($p < 0.05$).

Table 4: Effects of Aqueous Extract of *Balanites aegyptiaca* Fruit-Mesocarp on Liver function parameters of Alloxan-induced Diabetic Wistar Rats.

GROUP	ALT (U/L)	AST (U/L)	ALP (U/L)	T. Bilirubin (g/dL)	Protein (g/dL)	Albumin (g/dL)
1	5.33 ± 0.31	17.67 ± 0.24	45.0 ± 5.45^{b}	4.2 ± 1.1^{b}	13.90 ± 3.76^{b}	8.86 ± 1.87
2	6.67± 0.91	17.33 ± 1.13	54.4 ± 3.10^{a}	2.9 ± 0.8^{a}	15.77 ± 1.36^{a}	9.90 ± 2.43
3	5.33 ± 0.31	13.00 ± 2.19	42.4 ± 3.71^{b}	3.1 ± 0.2^{b}	19.49 ± 2.21^{a,b}	8.95 ± 1.31
4	11.67 ± 1.31^{a,b,c}	17.00 ± 1.73	47.4 ± 3.32^{b}	2.6 ± 0.3^{a}	16.04 ± 2.03^{a}	11.93 ± 0.90^{a,b,c}
5	12.00± 0.00^{a,b,c}	18.11 ± 1.11	45.3 ± 4.36^{b}	2.7 ± 1.0^{a}	18.94 ± 1.65^{a}	10.58 ± 2.31^{a,b,c}

Results are presented in Mean ± SEM (n = 5). Values with superscript a, b, and c means a significant difference when compared to group 1, 2 and 3 respectively ($p < 0.05$).

Effect on Haematological Parameters

Evaluation of haematological indices revealed that alloxan induction triggered a pronounced immune/inflammatory response, characterized by a significant elevation of White Blood Cell (WBC) count in the untreated diabetic group compared to the normal control (Table 5). Treatment with *B. aegyptiaca* extract significantly attenuated this leukocytosis in a dose-dependent manner. Red Blood Cell (RBC) count was significantly higher in the 400 mg/kg extract-treated group compared to all other experimental groups ($p < 0.05$). Interestingly, no statistically significant differences ($p > 0.05$) were observed among any of the groups regarding haemoglobin (HGB) concentration or haematocrit/packed cell volume (HCT). Mean corpuscular volume (MCV) was significantly higher in the metformin-treated group compared to both the untreated diabetic group and the extract-treated groups ($p < 0.05$).

Table 5: Effect of Aqueous Extract of *Balanites aegyptiaca* Fruit-Mesocarp on Some Haematological parameters in Alloxan-induced Diabetic Wistar Rats.

GROUP	WBC (10^9/L)	HGB (g/dL)	RBC (10^{12}/L)	HCT (%)	MCV (fL)
1	2.00 ± 0.71^{b}	10.57 ± 1.59	4.59 ± 0.36	26.20 ± 1.67^{b}	79.53 ± 5.17^{b}
2	5.89 ± 0.50^{a}	10.50 ± 1.18	5.60 ± 0.61	32.47 ± 3.07^{a}	69.53 ± 3.07^{a}
3	1.66 ± 0.29^{b}	12.60 ± 2.25	4.60 ± 0.41	$41.30 \pm 5.29^{a,b}$	$86.30 \pm 1.73^{a,b}$
4	4.40 ± 0.42^{a}	10.20 ± 0.17	4.71 ± 0.06	$31.9 \pm 1.44^{a,c}$	$67.77 \pm 2.48^{a,c}$
5	$3.27 \pm 0.20^{a,b}$	11.04 ± 2.05	$6.96 \pm 0.16^{a,c}$	$35.40 \pm 1.16^{a,c}$	$68.60 \pm 0.69^{a,c}$

Results are presented in Mean ± SEM (n = 5). Values with superscript a, b, and c means a significant difference when compared to group 1, 2 and 3 respectively ($p < 0.05$).

DISCUSSION

The therapeutic evaluation of the aqueous fruit-mesocarp extract of *Balanites aegyptiaca* (L.) Delile (Desert Date) highlights its complex role in metabolic and physiological homeostatic recovery in alloxan-induced diabetic Wistar rats. The findings confirm strong antidiabetic, weight-stabilizing, and hematoprotective potentials, alongside a dose-dependent effect on lipid and hepatic biomarkers. Alloxan selectively destroys pancreatic beta-cells via the generation of reactive oxygen species (ROS), resulting in a severe reduction in endogenous insulin secretion and subsequent profound hyperglycemia. This classic pathophysiological state was clearly reflected in the untreated diabetic group (Group 2), where Fasting Blood Sugar (FBS) escalated significantly over 28 days. The administration of *B. aegyptiaca* aqueous extract exhibited a clear, time-dependent antihyperglycemic effect. By Day 14 and Day 28, both the 200 mg/kg and 400 mg/kg doses completely normalized blood glucose levels, achieving parity with the baseline control group and the conventional biguanide metformin. This pronounced hypoglycemic capability is well-documented in ethnobotanical and systematic reviews of the plant (Odeniran, 2025). At a molecular level, recent investigations reveal that *B. aegyptiaca* fruit extracts manage blood glucose by upregulating the gene expression of hepatic insulin receptor A, glucose transporters (GLUT-2 and GLUT-4), and adipocyte leptin, while simultaneously downregulating pancreatic alpha-amylase activity to limit intestinal glucose absorption (El Deib, 2022). Computationally, phytomolecules within the fruit, such as flavonoids and steroidal saponins, mimic conventional antidiabetic drugs by modulating proteins associated with insulin sensitivity and glucose metabolism (Goulas *et al.*, 2022; Turaki *et al.*, 2025; Torres-González *et al.*, 2026).

Uncontrolled hyperglycemia initiates diabetic cachexia—a state characterized by severe muscle wasting and loss of structural proteins due to the body's inability to utilize glucose for energy. This explains the progressive weight loss observed in the untreated diabetic group. Treatment with *B. aegyptiaca* extract successfully reversed this wasting syndrome, resulting in progressive weight

stabilization and subsequent healthy weight gain comparable to metformin. This dynamic confirms an improvement in metabolic efficiency and a restoration of peripheral glucose utilization. The rich presence of natural sugars, essential amino acids, and high-energy macro-nutrients in the fruit pulp directly supports nutritional recovery and reverses catabolic tissue depletion (Abdelaziz *et al*., 2020).

The liver functions as the primary hub for metabolic homeostasis, and its structural integrity is frequently compromised by diabetic oxidative stress. In this study, serum alkaline phosphatase (ALP) activity rose significantly in the diabetic control group, indicating mild biliary or hepatocellular damage. The 400 mg/kg dose successfully restored ALP activity back to baseline, pointing to a standard hepatoprotective capacity typical of antioxidant-rich plant extracts. However, an unexpected finding emerged: alanine aminotransferase (ALT) activity was significantly elevated in both extract-treated groups compared to both controls, while aspartate aminotransferase (AST) remained statistically unaltered. While high ALT typically points to localized hepatocyte membrane permeability or leakage, the stable AST levels and the concurrent, statistically significant increase in serum total protein and albumin suggest a more nuanced metabolic adaptation rather than overt hepatotoxicity. Serum albumin, which increased exclusively in the extract groups, reflects enhanced hepatic synthetic capacity and protection against protein-energy wasting (Ansari *et al.*, 2022). The isolated increase in ALT may indicate an upregulation of gluconeogenic pathways or an adaptive metabolic shift driven by the high concentration of specific nitrogenous or phytochemical fractions unique to the *B. aegyptiaca* fruit mesocarp.

Diabetes mellitus is frequently accompanied by secondary dyslipidemia due to uninhibited lipolysis in adipose tissue, which accelerates the flux of free fatty acids to the liver. The lipid profile results presented here highlight a distinct, dose-dependent contrast: The 200 mg/kg dose (Group 4) unexpectedly caused elevations in total cholesterol, triglycerides, and LDL-cholesterol. The 400 mg/kg dose (Group 5) demonstrated an excellent, classic hypolipidemic profile, lowering total cholesterol and LDL while driving High-Density Lipoprotein (HDL) cholesterol to its maximum outperforming all other groups. This dosage dichotomy suggests that a threshold concentration of bioactive components is required to successfully trigger hypolipidemic pathways. Phytochemical screenings show that *B. aegyptiaca* fruit pulp contains complex mixtures of steroidal saponins, phenolic acids, and flavonoids (Abdelaziz *et al.*, 2020). When administered at lower doses, certain components (such as free fatty acids or saponin intermediates) may temporarily shift lipid mobilization into circulation. Conversely, at the higher dose (400 mg/kg), the collective, synergistic effect of these saponins and flavonoids actively suppresses HMG-CoA reductase and limits systemic lipid peroxidation, driving cholesterol clearance and maximizing cardioprotective HDL (El Deib, 2022).

Alloxan induction triggered an inflammatory and immune response, marked by a pronounced spike in White Blood Cell (WBC) counts (leukocytosis) in the untreated diabetic group. This is a common defensive reaction to systemic oxidative injury and tissue necrosis. Both doses of the *B. aegyptiaca* extract significantly attenuated this leukocytosis in a dose-dependent fashion, highlighting strong anti-inflammatory properties that calm the over activated immune response. Furthermore, Red Blood Cell (RBC) counts were maximized in the 400 mg/kg extract-treated group, outperforming all other experimental groups. The lack of negative alterations in hemoglobin (HGB) concentrations and hematocrit (HCT/PCV) across the cohorts confirms that the extract lacks hemolytic toxicity. Instead, the boost in RBC counts points to a direct hematoprotective or erythropoietin-stimulating effect, likely driven by the antioxidant polyphenols in the fruit pulp that defend red cell membranes against premature lipid peroxidation and fragility (Abdelaziz *et al.*, 2020; Djaoudene, 2026).

Conclusion

The aqueous fruit-mesocarp extract of *Balanites aegyptiaca* acts as an effective therapeutic agent against alloxan-induced diabetic complications. It completely normalizes fasting blood glucose, reverses diabetic cachexia, calms immune inflammation, and provides potent cardioprotection by optimizing HDL at a higher dose (400 mg/kg). While the isolated elevation in ALT warrants careful toxicological monitoring, the corresponding improvements in serum albumin, ALP baseline restoration, and overall hematoprotection suggest a highly promising, multifaceted therapeutic window for the management of diabetes and its secondary complications.

Conflict of Interest

The authors declare no conflict of interest.

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