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Original Research Article

EVALUATION OF THE TOXICITY, HYPOGLYCAEMIC AND HEPATOPROTECTIVE POTENTIAL OF THE PHENOLIC EXTRACT OF *Picralima nitida* IN DIABETIC WISTAR RATS

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ABSTRACT

Despite the widespread knowledge of the use of Picralima nitida in traditional medicine, its phenolic-rich bioactive component remains inadequately researched for safety and organ-protective benefits in management of diabetes. Therefore, this study investigated the toxicity, hypoglycaemic and hepatoprotective effects of the phenolic extract of Picralima nitida leaves in streptozotocin-induced diabetic Wistar rats. henolic constituents were extracted through hydro-methanolic maceration, solvent partitioning, and ferric-chloride confirmation, while acute toxicity was evaluated using Lorke's method. Eighteen (18) rats were allocated into six groups and treated with phenolic extract (200, 400, 600 mg/kg), glibenclamide (3 mg/kg) as standard drug, or saline (Normal control) for 14 days. Fasting blood glucose, body weight, hematological indices (RBC, PCV, Hb, WBC, PLT, MCV, MCH, MCHC), and liver function biomarkers (ALT, AST, ALP, bilirubin fractions, total protein, albumin, globulin) were determined using standard glucometric, hematology analyzer, and spectrophotometric procedures. Data were collected in triplicate and analyzed using repeated-measures ANOVA and t-tests ($p < 0.05$). Result showed that P. nitida phenolic extract exhibited a high safety profile with LSD greater than 5000 mg/kg. Acute and sub-acute studies showed significant, dose-dependent glucose reductions, with the 600 mg/kg dose producing the strongest effect (up to 27.6% reduction at 4h), surpassing glibenclamide. Extract treatment attenuated diabetes-induced weight loss and produced marked hematological improvements: RBC, PCV, and Hb increased significantly across all doses, with near-normalization at 600 mg/kg; WBC and platelet elevations were significantly reduced ($P<0.05$), MCV, MCH, and MCHC showed partial improvement. Hepatic injury markers improved significantly, as ALT, AST, ALP, and bilirubin levels decreased significantly, while total protein, albumin, and globulin increased in a dose-dependent manner, reflecting restored hepatocellular integrity. Phenolic extract of P. nitida was found to demonstrate potent hyperglycaemic and hepatoprotective effects with high safety, supporting its therapeutic potential as a plant-based adjunct in diabetes management.

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INTRODUCTION

The global burden of metabolic disorders continues to intensify, with diabetes standing out as one of the most rapidly expanding conditions. Epidemiological projections indicate that the number of adults aged 20–79 living with the disease neutralize the gastric acid while is steadily increasing, rising from 285 million in 2010 to a projected 439

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million by 2030 [1–3]. The bulk of these diseases are caused by type 2 diabetes, which is currently a leading cause of early death in high-income areas [4]. Longer life expectancy, urbanization, decreased physical exercise, and genetic susceptibility have all contributed to diabetics's worldwide rise to epidemic levels [5]. Over 90% cases of diabetes are type 2, which is caused by decreased insulin action, increasing β-cell loss, and changes in metabolic pathways [6]. Type 1 diabetes originates from autoimmune-mediated death of the pancreatic β-cells responsible for insulin generation [7,8]. Diabetes significantly affects hepatic biomarkers by interfering with the liver's regular functions in controlling cholesterol and glucose [9]. Under persistent hyperglycemia, the liver becomes sensitive to oxidative damage, inflammatory signaling, and mitochondrial dysfunction [10,11]. These pathogenic alterations lead to the release of intracellular enzymes into the bloodstream, leading to elevations in alanine aminotransferase, aspartate aminotransferase (AST), and alkaline phosphatase (ALP) [12,13]. Their rise is indicative of compromised structural integrity, decreased metabolic efficiency, and damage to the hepatocyte membrane. These biomarkers offer excellent information into the level of systemic metabolic imbalance in diabetes and serve as essential indicators when evaluating the organ-protective potential of developing antidiabetic medicines.

Patients with diabetes are managed by adopting a healthy lifestyle, using oral drugs, or daily insulin injections to assist in controlling their blood sugar levels [14,15]. Conventional drugs have been reported for undesirable effects, high cost, and limited accessibility to low- and medium-income countries [16,17]. These gaps have stimulated interest in medicinal plants rich in bioactive phytochemicals, that possess alternative therapeutic effects. *Picralima nitida*, sometimes known as "Ogbono bitter" or "Akuamma," is a West African medicinal plant that has long been used to cure discomfort, fever, gastrointestinal problems, malaria, and metabolic disorders [18–25]. There is a need to investigate these individual bioactive compounds to determine their specific efficacy, therapeutic potential, and safety profiles, as well as to establish their contribution to the plant's overall pharmacological activity. Therefore, this work aims to investigate the toxicity, hypoglycaemic and hepatoprotective properties of the phenolic extract of *Picralima nitida* utilizing pertinent biochemical indicators in diabetic Wistar rats

MATERIAL AND METHODS

Plant material

Fresh *Picralima nitida* leaves were obtained from Ekeja market in Uburu, Ebonyi State. The plant specimens were identified and verified at the Department of Applied Biology, Enugu State University of Science and Technology (ESUT), Enugu, Nigeria. A voucher specimen was deposited in the departmental herbarium under voucher number ESUT/AB/PN/2025/025.

Chemicals and Equipment Used for the Study

Analytical-grade chemicals were used throughout the study. Alloxan monohydrate, ethanol, and buffered formalin were purchased from Sigma-Aldrich (St. Louis, MO, USA). Distilled water was obtained from a local supplier in Aba, Abia State, Nigeria. The equipment used included a Micro Hematocrit Centrifuge (Model DM1424, DLAB Scientific Co., Beijing, China), Accu-Chek Active Glucometer (Model Active, Roche Diagnostics GmbH, Mannheim, Germany), MS-H280-Pro Magnetic Stirrer (DLAB Scientific Co., Beijing, China), Pioneer PX224 Electronic Analytical Balance (OHAUS Corporation, Parsippany, NJ, USA), and Whatman No. 1 filter paper (Cytiva/Whatman™, Marlborough, MA, USA), SYSMEX KX-21 automated hematology analyzer. Other laboratory materials included coloured glass bottles, funnels, perforated aluminium cages, feed plates, gloves, incubation tubes, capillary tubes, and masking tape.

Preparation of *Picralima nitida* leaves

Fresh *Picralima nitida* leaves were washed, air-dried, and ground into a fine powder using a sterilized grinder [26]. The powdered leaves were defatted with n-hexane (1:5 w/v) for 24–48 hrs with occasional stirring, then filtered and dried at room temperature or in a 40–45 °C oven before further use.

Extraction and bioactive constituents of Phenol from *P. nitida* leaves

Phenolic constituents were extracted using a modified hydro-methanolic maceration and solvent-partitioning method according to [27]. Twenty grams of powdered, air-dried *Picralima nitida* leaves were macerated in 200 mL of 80% methanol for 48h with occasional shaking. The mixture was filtered, and the filtrate concentrated at 40–50 °C to yield an aqueous residue. Non-polar compounds were removed with n-hexane, and the aqueous phase was repeatedly partitioned with ethyl acetate to extract medium-polarity phenolics. The combined organic layers were evaporated under reduced pressure to obtain the phenolic-rich extract, stored at 4 °C in an amber vial. Phenolic presence was confirmed using the ferric chloride test. Percentage yield was determined using Equation 1.

$$\text{Percentage yield (\%)} = \frac{Q}{W} \times 100 \quad (1)$$

where Q is the mass of the dried phenolic fraction and W is the initial plant material mass.

Experimental Animals

Adult male Wistar rats (160–200 g) were obtained and acclimatized for 14 days under standard laboratory conditions with unrestricted access to feed and water. The study protocol was approved by the Research Ethics Committee of Enugu State University of Science and Technology (ESUT), Enugu, Nigeria (Approval No. ESUT/REC/2025/057). Following an overnight fast (10–12 h), diabetes was induced by intraperitoneal administration of streptozotocin (50 mg·kg^{-1}) freshly prepared in cold citrate buffer (pH 4.5). To minimize acute hypoglycaemia, rats received 5% glucose solution for 24 h after streptozotocin injection. Fasting blood glucose was measured 72 h post-

induction, and animals with glucose levels ≥250 mg·dL^{-1} were considered diabetic and included in the study. All procedures complied with established guidelines for the care and use of laboratory animals [28].

Experimental design for the hypoglycemic study

A total of eighteen (18) Wistar albino rats were used and grouped into 6 (A-F) of three (3) rats per group and were treated according to the order below: Groups B-F were induced with diabetes using streptozotocin (50 mgkg ^{1}) and subsequently treated with phenol extract at 200, 400, and 600 mg/kg as indicated below.

Group A: Normal control (0.2 ml normal saline daily + feed)
Group B: Diabetic control (0.2 ml normal saline daily + feed)
Group C: Diabetic + Glibenclamide (3mg/kg)
Group D: Diabetic + Phenol (200 mg/kg)
Group E: Diabetic + Phenol (400 mg/kg)
Group F: Diabetic + Phenol (600 mg/kg)

Fasting blood glucose was assessed 72h later using a digital glucometer (Accu-Check Active®) via tail-vein sampling, and only rats with values ≥ 160 mg/dL [29], were included as diabetic. Treatments began on day 4 post-induction and continued for 14 days. Group B received only 0.2 mL normal saline daily. Group C was administered glibenclamide (3 mg/kg). Groups D, E, and F were given the phenolic extract at doses of 200, 400, and 600 mg/kg b.w., respectively.

Acute Toxicity (LD_{50}) Study of *Picralima nitida* Leaves Phenolic Extract

Acute toxicity was determined using the LD_{50} procedure described by Lorke's method [30]. A total of 18 Wistar rats (160–200 g) were used for the acute toxicity evaluation of the phenol extracts. The assessment followed a two-phase procedure. In Phase I, nine rats were divided into three groups and received oral doses of 10, 100, and 1000 mg/kg of the crude extract. Animals were observed for 24 hrs for signs of toxicity, including tremors, lethargy, convulsions, or mortality. Phase II involved another set of nine rats, grouped similarly, and administered higher doses (1600, 2900, and 5000 mg/kg) of the respective extracts. Observations continued for 24h and were extended to 168hrs to confirm delayed toxicity responses. The median lethal dose (LD_{50}) of the crude extract of *Picralima nitida* leaves was calculated using the formula adopted by [31] as presented in equation 2.

$$LD50 = \sqrt{(least dose with mortality \times highest dose without mortality)} \quad (2)$$

Determination of hematological parameters

Hematological parameters were evaluated using the method in [32]. 50mL of blood samples were introduced into the equipment, and it automatically employs the differences in characteristics possessed by each of the blood components to distinguish and estimate them. Hematological indices, including RBC (×10^{6}/mm³), PCV (%), Hb (g/dL), WBC (×10³/mm³), PLT (×10³/mm³), MCV (fL), MCH (pg), and MCHC (g/dL), were determined using the SYSMEX KX-21 automated hematology analyzer

Analysis of Liver Function Indices

Liver function indices were evaluated by determining the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and the concentrations of total, direct, and indirect bilirubin using standard commercial diagnostic kits. Enzyme activities were quantified spectrophotometrically using commercial assay kits (Randox Laboratories Ltd., Crumlin, County Antrim, United Kingdom) according to the manufacturer's instructions, while bilirubin concentrations were determined using the diazo reaction method with corresponding Randox reagent kits.

Statistical Analysis

The data obtained were subjected to ANOVA with repeated measures and t-test. Significant differences were accepted at $p < 0.05$. This analysis was carried out using IBM SPSS Statistics version 23.

RESULTS

Acute toxicity of phenolic extract of *Picralima nitida* leaf

The acute toxicity results of the phenolic extracts of *Picralima nitida* seeds are shown in Tables 1. No mortality occurred in either phase of the LD_{50} evaluation. In Phase 1, oral doses of 10, 100, and 1000 mg/kg produced no observable signs of toxicity. Based on this, higher doses of 1600, 2900, and 5000 mg/kg were administered in Phase 2, and all animals survived without adverse effects. These findings demonstrate a wide safety margin, as no lethality was recorded even at 5000 mg/kg. The LD_{50} is therefore estimated to exceed 5000 mg/kg body weight, classifying the extracts as practically non-toxic under standard acute toxicity criteria.

Table 1: Result of LD_{50} for alkaloid extract of *Picralima nitida* Seeds

Group	No. of Mice	Dose (mg/kg)	No. of death	No. of survival
1	3	10	0	3
2	3	100	0	3
3	3	1000	0	3
Phase 2 LD_{50} results				
1	3	1600	0	3

2	3	2900	0	3
3	3	5000	0	3

Acute anti-hyperglycemic study

Figure 1 shows the acute changes in blood glucose concentrations following single-dose administration of the phenolic extract of *Picralima nitida* in streptozotocin-induced diabetic rats. In the diabetic control group, blood glucose levels increased by 2.32% and 4.64% at 2 h and 4 h, respectively, relative to baseline. Treatment with glibenclamide (3 mg/kg) reduced blood glucose concentrations from 246.00 ± 50.48 mg/dL at 0 h to 238.00 ± 54.84 mg/dL at 2 h and 205.00 ± 37.64 mg/dL at 4 h, corresponding to decreases of 3.25% and 16.67%, respectively. Administration of the phenolic extract at 200 mg/kg reduced blood glucose levels by 9.68% and 22.58% at 2 h and 4 h, respectively, while the 400 mg/kg dose produced reductions of 10.00% and 23.33%. The 600 mg/kg dose elicited the greatest response, with reductions of 13.79% at 2 h and 27.59% at 4 h. The decrease observed at 600 mg/kg was significant ($P < 0.01$) compared with the diabetic control group.

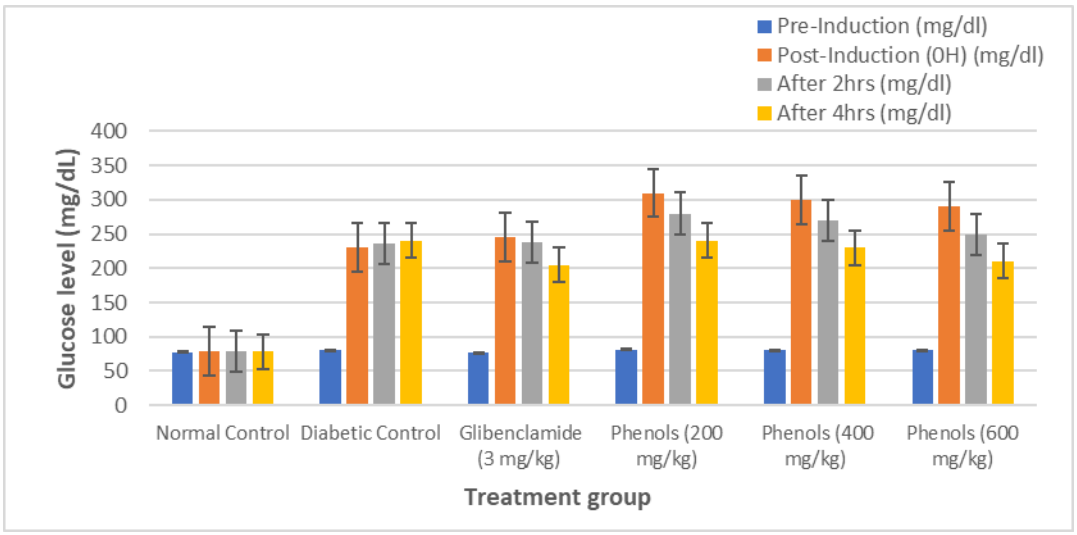


***Figure 1**: Acute anti-hyperglycemic potential of Picralima nitida phenolic leaf extract on diabetic Wistar rats*

Sub-acute anti-hyperglycaemic study

Figure 2 presents the post-induction and post-treatment blood glucose concentrations following administration of the phenolic extract of *Picralima nitida*. At 0 h post-induction, the diabetic control group showed significantly higher blood glucose levels than the normal control group, confirming successful induction of diabetes. Treatment with glibenclamide (3 mg/kg) significantly reduced blood glucose concentration compared with the diabetic control group ($P < 0.05$). Administration of the phenolic extract at 200, 400, and 600 mg/kg produced significant reductions in blood glucose levels relative to the diabetic control group ($P < 0.05$). The glucose-lowering effect increased with dose, with the 600 mg/kg group exhibiting the greatest reduction among the extract-treated groups.

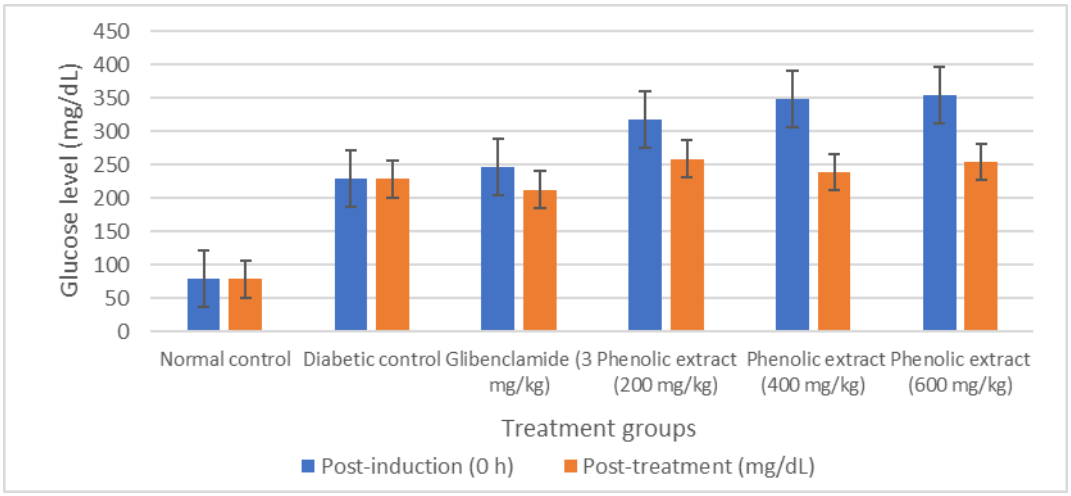


***Figure 2**: Sub-acute anti-hyperglycemic potential of Picralima nitida phenolic leaf extract on diabetic Wistar rats*

Effect of treatments on body weights of diabetic rats

The effect of *P. nitida* phenolic extract on diabetic wistar rats is presented in Figure 3. Following diabetes induction, the

Diabetic Control group exhibited a progressive decline in body weight, decreasing from 139.7 ± 7.8 g (mean ± SD) pre-induction to 134.3 ± 6.9g post-induction, representing a 3.8% loss. In contrast, groups treated with glibenclamide (3 mg/kg), phenolic extracts at 200, 400, and 600 mg/kg showed a partial mitigation of weight loss, with post-induction weights of 121.7 ± 3.6 g, 121.5 ± 3.9 g, 119.3 ± 3.6 g, and 120.5 ± 6.6 g, respectively, indicating a statistically significant ($p < 0.05$) weight differences between treated groups and Diabetic Control. The highest phenol dose (600 mg/kg) showed comparable efficacy to glibenclamide in restoring body weight although the difference was not significant (P>0.05).

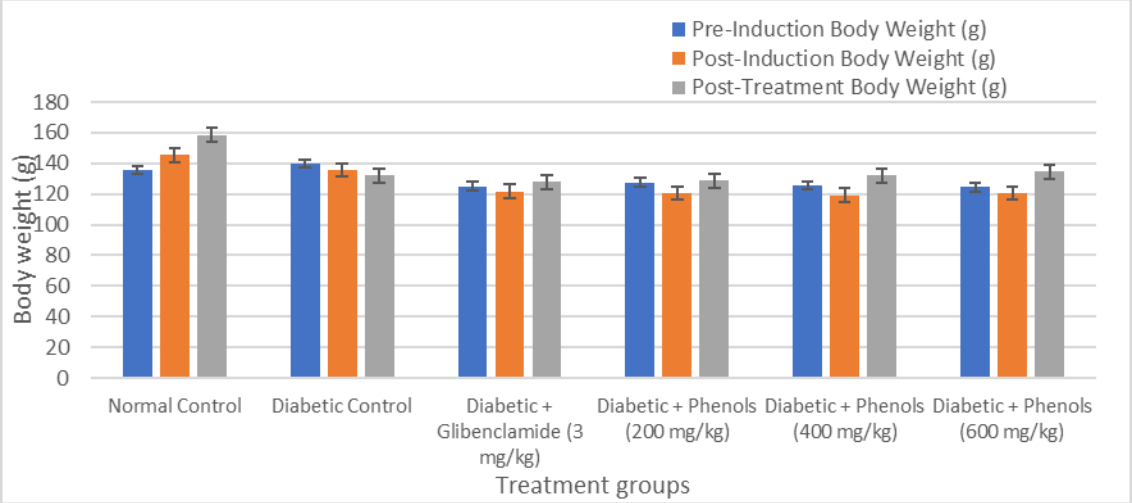


***Figure 3**: Effect of Picralima nitida phenolic leaf extract on body weight of diabetic Wistar rats*

Effects of treatments on hematological parameters of diabetic rats

The effects of the phenolic extract of *Picralima nitida* on haematological parameters of diabetic Wistar rats are presented in Figures 4–11. As shown in Figure 4, red blood cell (RBC) count differed significantly among the groups.

Treatment with glibenclamide (MD = 0.57, $p = 0.001$) and the phenolic extract at 200 mg/kg (MD = 0.83, $p < 0.001$), 400 mg/kg (MD = 1.09, $p < 0.001$), and 600 mg/kg (MD = 1.19, $p < 0.001$) significantly increased RBC count relative to the diabetic control group. The highest RBC value was observed in the 600 mg/kg extract-treated group.

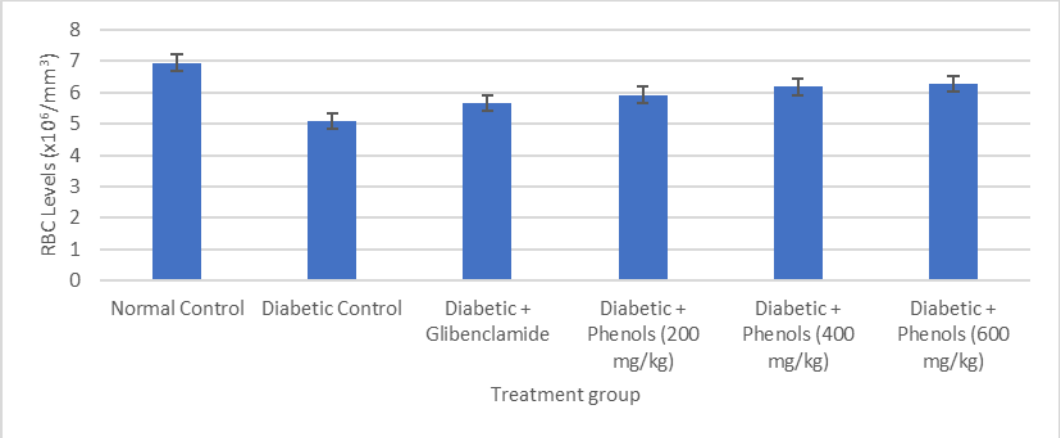


***Figure 4**: Effect of Picralima nitida phenolic leaf extract on red blood count (RBC) of diabetic Wistar rats*

Packed cell volume (PCV) results are presented in Figure 5. The diabetic control group showed significantly reduced PCV compared with the normal control (MD = 11.33, $p < 0.001$). Treatment with glibenclamide (MD = 4.67, $p = 0.001$) and the phenolic extract at 200 mg/kg (MD = 7.00, $p < 0.001$), 400 mg/kg (MD = 8.33, $p < 0.001$), and 600 mg/kg (MD = 9.33, $p < 0.001$) significantly increased PCV relative to the diabetic control. The PCV value in the 600 mg/kg group was not significantly different from that of the normal control (MD = −2.00, $p = 0.192$).

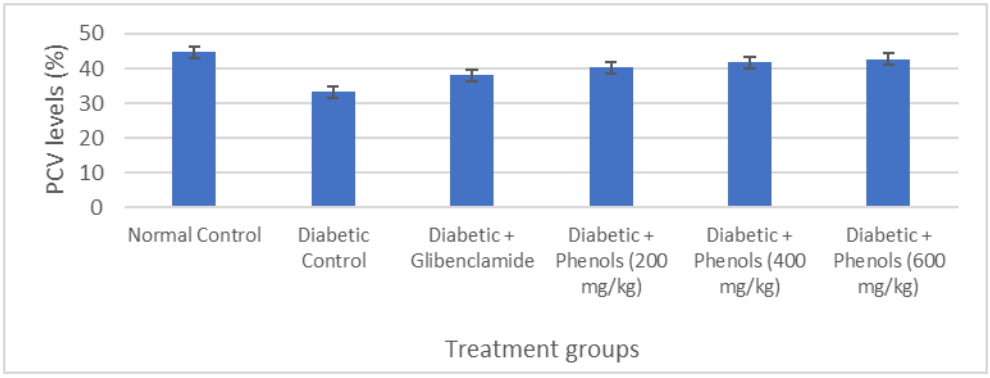


***Figure 5**: Effect of Picralima nitida phenolic leaf extract on PCV of diabetic Wistar rats*

Figure 6 shows the haemoglobin (Hb) concentrations of the experimental groups. Diabetic rats exhibited significantly lower Hb levels than the normal control group (MD = 5.00, $p < 0.001$). Administration of glibenclamide (MD = 1.70, $p = 0.003$) and the phenolic extract at 200 mg/kg (MD = 2.37, $p < 0.001$), 400 mg/kg (MD = 2.90, $p < 0.001$), and 600 mg/kg (MD = 3.50, $p < 0.001$) significantly increased Hb concentration compared with the diabetic control group.

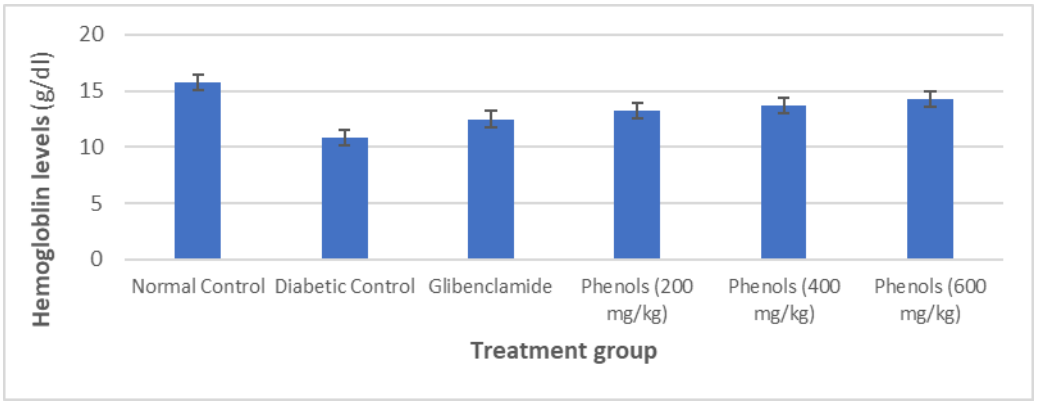


***Figure 6:** Effect of Picralima nitida phenolic leaf extract on hemoglobin* (Hb) *level of diabetic Wistar rats*

The effect of the extract on white blood cell (WBC) count is shown in Figure 7. Relative to the diabetic control group, glibenclamide (MD = −0.76, $p = 0.015$), phenolic extract at 200 mg/kg (MD = −0.70, $p = 0.026$), 400 mg/kg (MD = −0.83, $p = 0.008$), and 600 mg/kg (MD = −1.23, $p < 0.001$) significantly reduced WBC count, with the greatest reduction observed at 600 mg/kg.

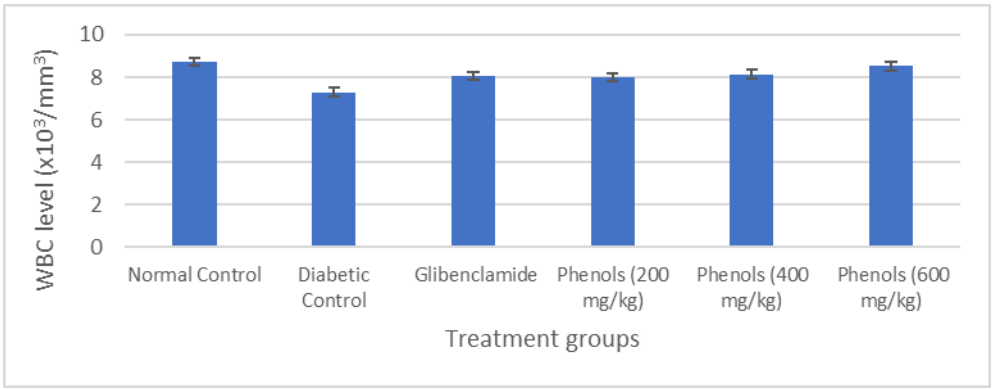


Figure 7: Effect of *Picralima nitida* phenolic leaf extract on white blood count (WBC) of diabetic Wistar rats

Figure 8 presents platelet (PLT) counts in the experimental groups. Although platelet count was higher in the diabetic control group than in the normal control group, the difference was not significant (MD = 17.67, $p = 0.056$). Treatment with glibenclamide (MD = −21.33, $p = 0.018$) and the phenolic extract at 200 mg/kg (MD = −27.00, $p = 0.003$), 400 mg/kg (MD = −25.00, $p = 0.006$), and 600 mg/kg (MD = −28.00, $p = 0.002$) significantly reduced platelet count relative to the diabetic control group.

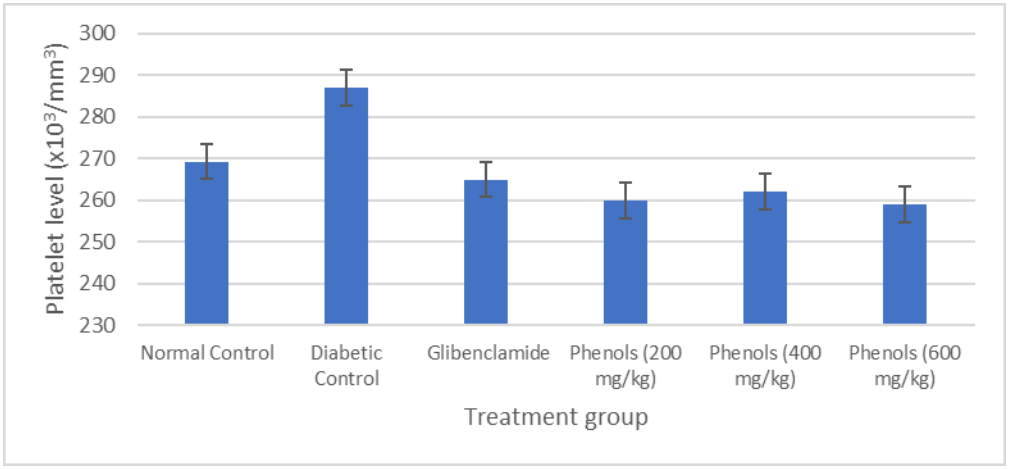


***Figure 8**: Effect of Picralima nitida phenolic leaf extract on platelet level of diabetic Wistar rats*

Mean corpuscular volume (MCV) values are shown in Figure 9. The phenolic extract-treated groups exhibited higher MCV values than the normal control group, with significant increases observed at 200 mg/kg (MD = 3.80, p = 0.003) and 600 mg/kg (MD = 3.67, p = 0.004).

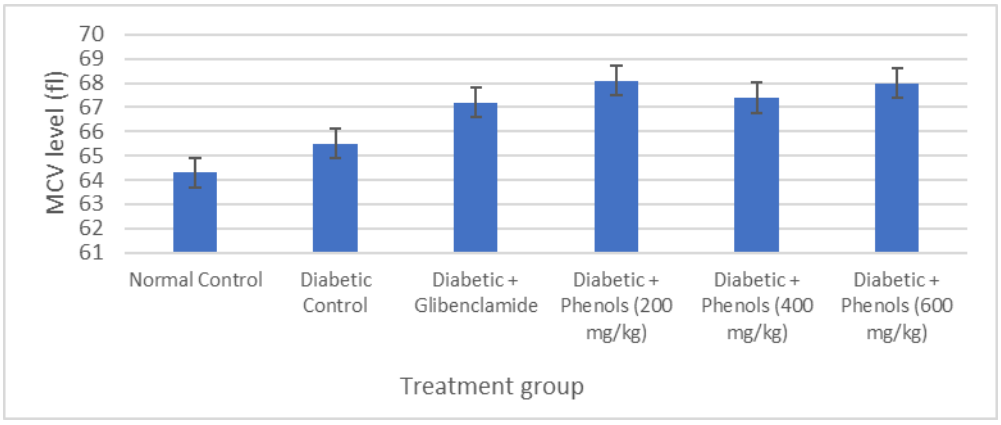


***Figure 9**: Effect of Picralima nitida phenolic leaf extract on MCV level of diabetic Wistar rats*

As shown in Figure 10, mean corpuscular haemoglobin (MCH) differed significantly between the diabetic and normal control groups (MD = 1.53, p = 0.018). Among the treatment groups, only the 600 mg/kg dose significantly increased MCH relative to the diabetic control group (MD = −1.50, p = 0.021).

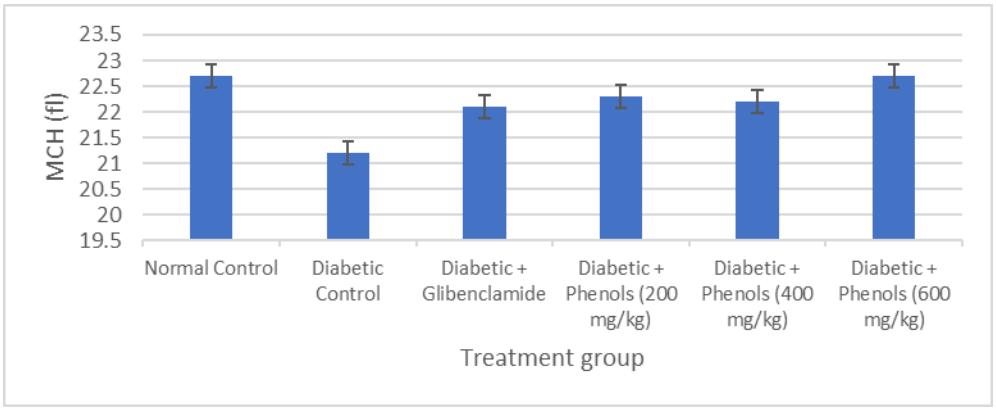


***Figure 10**: Effect of Picralima nitida phenolic leaf extract on MCH level of diabetic Wistar rats*

Figure 11 presents the mean corpuscular haemoglobin concentration (MCHC) values. The diabetic control group exhibited significantly lower MCHC than the normal control group (MD = 2.97, p < 0.001). Treatment with glibenclamide

and all doses of the phenolic extract significantly increased MCHC compared with the diabetic control group ($p \leq 0.001$). The 600 mg/kg dose produced values closest to those of the normal control group (MD = −0.93, $p = 0.072$).

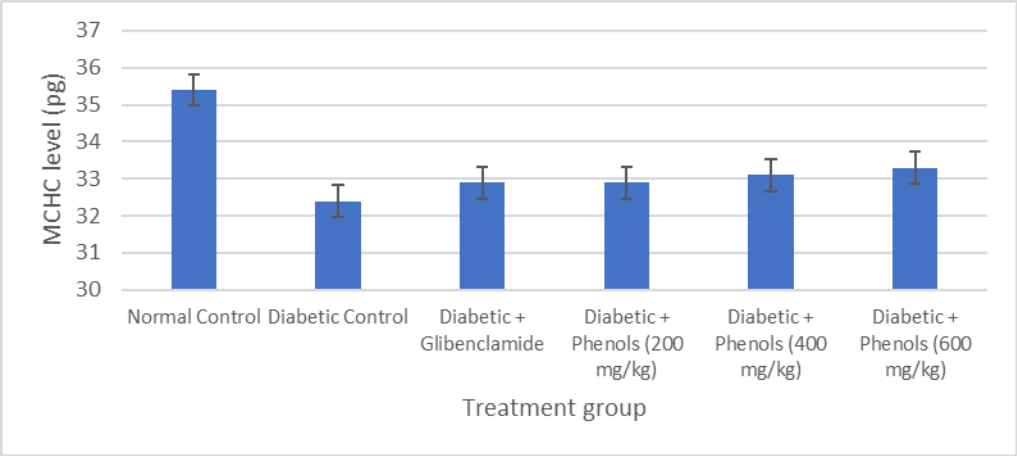


Figure 11: Effect of *Picralima nitida* phenolic leaf extract on MCHC level of diabetic Wistar rats

Effects of treatments on liver function parameters of diabetic rats

Figure 12 presents the effect of *P. nitida* on the liver function parameters of diabetic rats. Induction of glibenclamide treatment significantly increased total protein concentration compared with the diabetic control group (MD = 0.76 g/dL, $p < 0.01$). Phenolic extract was found to significantly increased total protein at 200 mg/kg (MD = 0.56 g/dL, $p < 0.001$), 400 mg/kg (MD = 0.66 g/dL, $p < 0.001$), and 600 mg/kg (MD = 0.67 g/dL, $p < 0.001$). However, the differences among the treated groups were not statistically significant ($p > 0.05$).

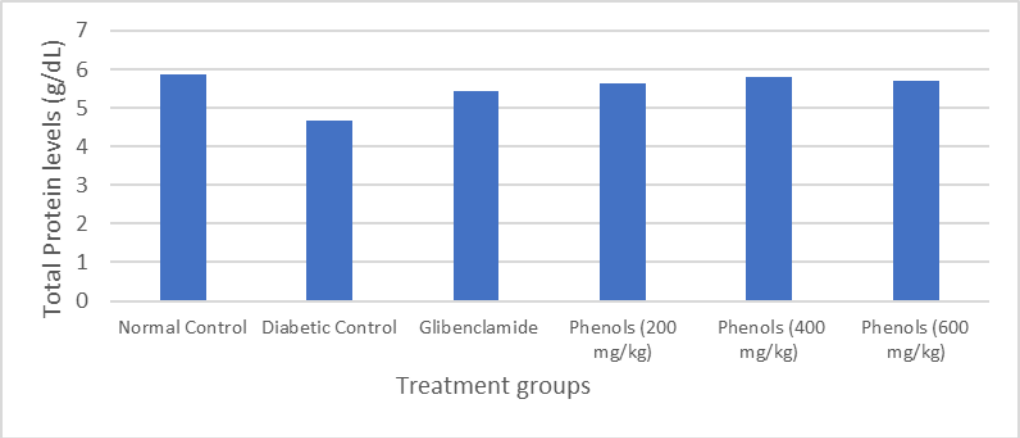


Figure 12: Effect of *Picralima nitida* phenolic leaf extract on total protein of diabetic Wistar rats

The albumin concentration was significantly lower in the diabetic control group than in the normal control group ($p < 0.001$) as shown in Figure 13. Glibenclamide significantly increased albumin concentration compared with the diabetic control group (MD = 0.25 g/dL, $p < 0.01$). The phenolic extract at 200, 400, and 600 mg/kg also significantly increased albumin relative to the diabetic control ($p < 0.05$). The greatest improvement was observed at 600 mg/kg; however, the differences among the extract-treated groups were not statistically significant ($p > 0.05$).

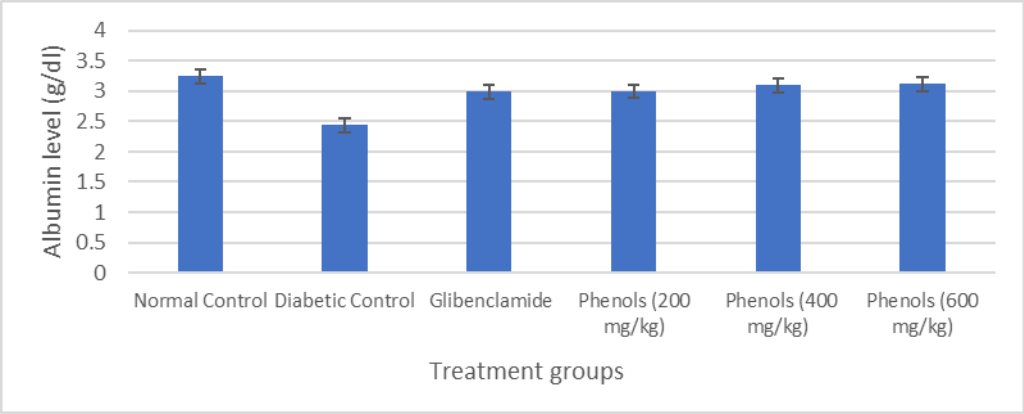


Figure 13: Effect of *Picralima nitida* phenolic leaf extract on albumin level of diabetic Wistar rats

Figure 14 shows a significant reduction in globulin concentration in the diabetic control group compared with the normal control group ($p < 0.001$). Administration of the phenolic extract at 200, 400, and 600 mg/kg significantly increased globulin concentration relative to the diabetic control group ($p < 0.05$). The highest effect was observed at 200 mg/kg.

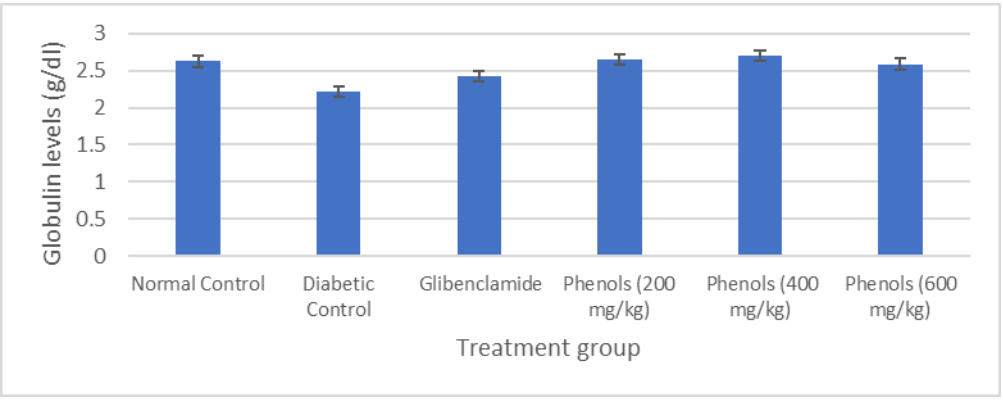


Figure 14: Effect of *Picralima nitida* phenolic leaf extract on globulin level of diabetic Wistar rats

Figure 15 shows a significant elevation of ALT activity in the diabetic control group compared with the normal control group ($p < 0.001$). Glibenclamide and the phenolic extract at 200, 400, and 600 mg/kg significantly reduced ALT activity relative to the diabetic control group ($p < 0.01$). The lowest ALT activity among the extract-treated groups was observed at 600 mg/kg. However, differences among the three extract doses were not statistically significant ($p > 0.05$).

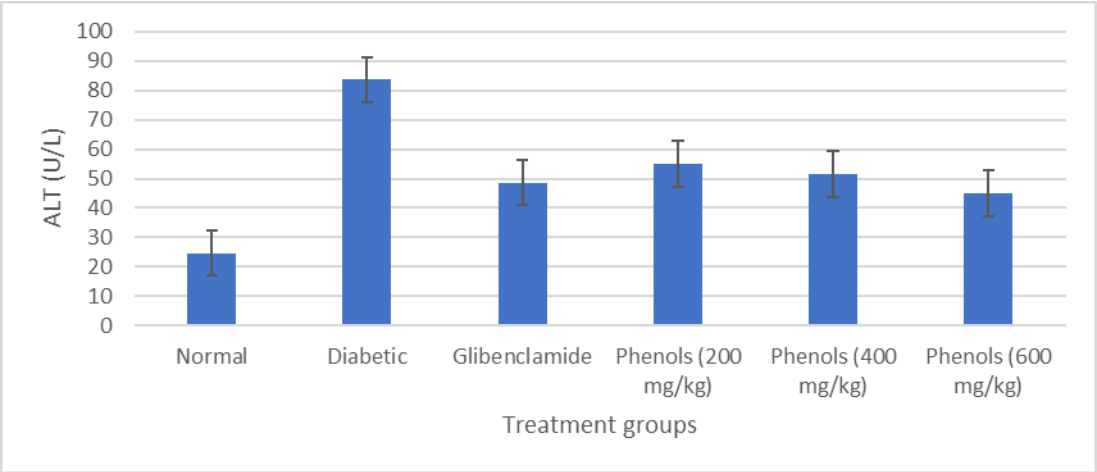


Figure 14: Effect of *Picralima nitida* phenolic leaf extract on globulin level of diabetic Wistar rats

Figure 16 shows that AST activity was 90.67 U/L in the diabetic control group compared with 35.67 U/L in the normal control group (MD = 55.00 U/L). Treatment with glibenclamide reduced AST activity to 47.00 U/L (MD =

−43.67 U/L, $p < 0.05$). The phenolic extract reduced AST activity to 48.00 U/L at 200 mg/kg (MD = −42.67 U/L), 46.67 U/L at 400 mg/kg (MD = −44.00 U/L), and 49.67 U/L at 600 mg/kg (MD = −41.00 U/L), with all treatment groups showing significant reductions relative to the diabetic control ($p < 0.05$). The 400 mg/kg group recorded the lowest AST value among the extract-treated groups.

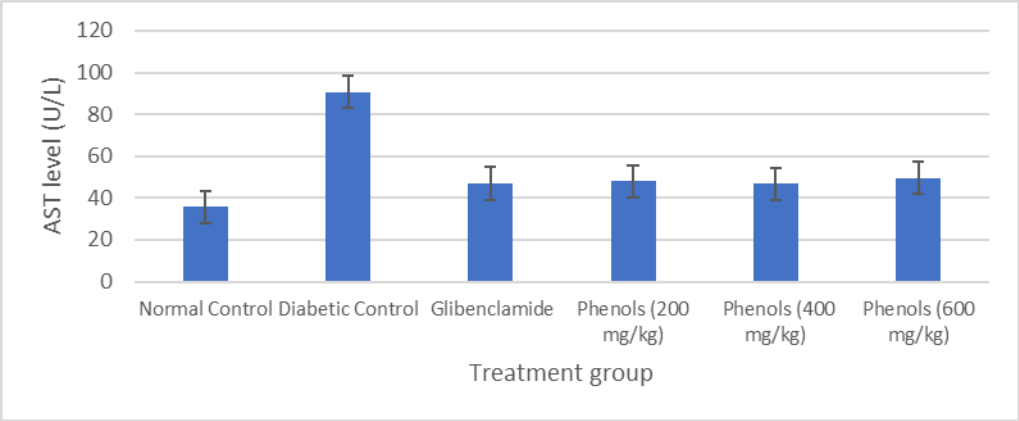


Figure 16: Effect of *Picralima nitida* phenolic leaf extract on AST level of diabetic Wistar rats

Figure 17 shows that ALP activity increased from 74.00 U/L in the normal control group to 128.33 U/L in the diabetic control group (MD = 54.33 U/L). Treatment reduced ALP activity to 92.00 U/L at 200 mg/kg (MD = −36.33 U/L), 93.33 U/L at 400 mg/kg (MD = −35.00 U/L), and 88.00 U/L at 600 mg/kg (MD = −40.33 U/L). Glibenclamide produced an ALP activity of 93.33 U/L (MD = −35.00 U/L). The reductions produced by the phenolic extract were significant compared with the diabetic control group ($p < 0.05$), with the lowest ALP activity observed at 600 mg/kg.

Bilirubin: Figure 18 shows that bilirubin concentration was higher in the diabetic control group than in the normal control group (MD = 0.57 mg/dL). Treatment with glibenclamide reduced bilirubin concentration relative to the diabetic control group (MD = −0.35 mg/dL). The phenolic extract also reduced bilirubin at 200, 400, and 600 mg/kg, with MD values of −0.42, −0.46, and −0.46 mg/dL, respectively. The corresponding bilirubin concentrations for the extract-treated groups ranged from 0.77 to 0.80 mg/dL. However, the treated groups did not completely return to the normal control level.

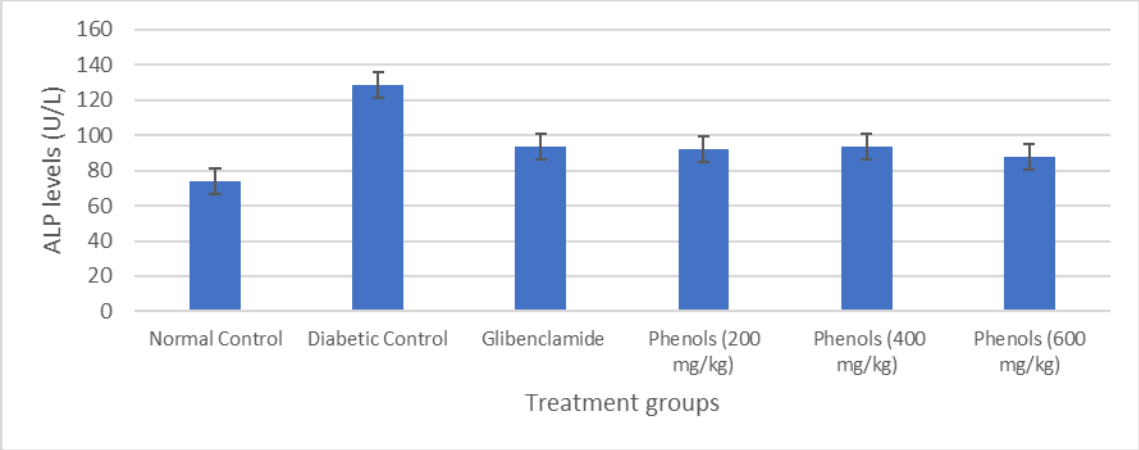


Figure 17: Effect of *Picralima nitida* phenolic leaf extract on ALP level of diabetic Wistar rats

The effect of the phenolic extract of *Picralima nitida* on total bilirubin levels in diabetic Wistar rats is presented in Figure 18. The diabetic control group exhibited the highest bilirubin concentration (1.22 ± 0.03 mg/dL) compared with the normal control (0.65 ± 0.03 mg/dL). Treatment with glibenclamide (3 mg/kg) reduced bilirubin to 0.87 ± 0.02 mg/dL. Similarly, the phenolic extract produced a progressive reduction in bilirubin concentration, from 0.94 ± 0.02 mg/dL at 200 mg/kg to 0.86 ± 0.03 mg/dL at 400 mg/kg and 0.79 ± 0.04 mg/dL at 600 mg/kg. The lowest bilirubin concentration among the extract-treated groups was therefore observed at 600 mg/kg, indicating a dose-related improvement in bilirubin status

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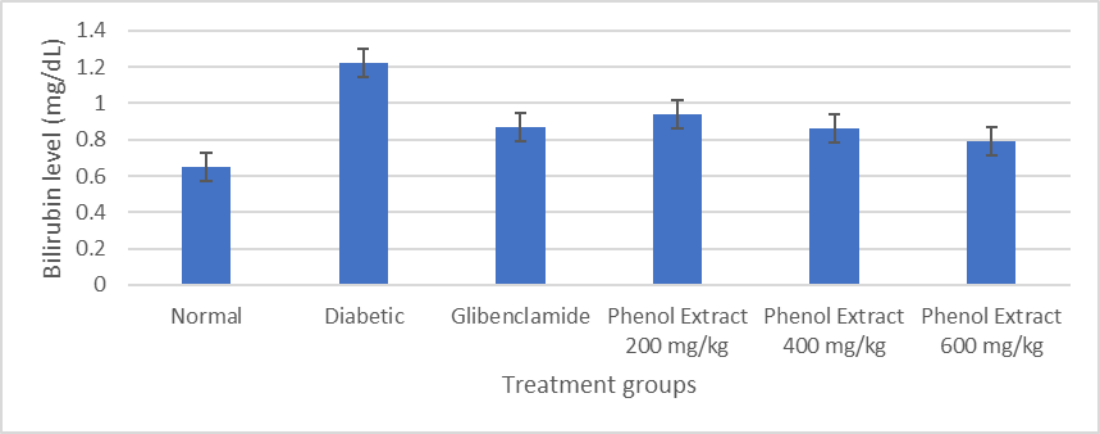


Figure 18: Effect of *Picralima nitida* phenolic leaf extract on bilirubin level of diabetic wistar rats

DISCUSSION

The observed reduction in blood glucose concentration following administration of the phenolic extract of *P. nitida* demonstrates its antihyperglycaemic activity in streptozotocin-induced diabetic rats. The progressive decrease in glucose levels across the treatment groups suggests a dose-dependent effect, indicating that higher concentrations of the extract may possess greater glucose-lowering efficacy as notably in 600 mg/kg. Managing the rise in blood glucose after meals is a major part of diabetes care, and shows the ways that the body handles glucose after a pure glucose load is very similar to its response after a mixed meal containing carbohydrates, fats, and proteins [33]. After eating, the liver is the first organ to experience the sharp increase in glucose and insulin [11]. The acute antihyperglycemic effects observed in this study, particularly the superior glucose-lowering activity of the 600 mg/kg dose compared with glibenclamide, supports the potency of the phenolic extract. This is consistent with reports that *P. nitida* contains phenolic constituents capable of improving glycemic indices through antioxidant-mediated β-cell protection, inhibition of carbohydrate-hydrolyzing enzymes, and enhancements in insulin sensitivity [29]. De Campos et al. [34] demonstrated significant hypoglycemic and metabolic-restorative activity of *P. nitida* extract in diet-induced diabetic models. Beyond *P. nitida*, phenolic compounds in general are well documented for their antihyperglycemic action through α-glucosidase inhibition, modulation of GLUT4 translocation, and suppression of hepatic gluconeogenesis [35].

The phenolic extract of *P. nitida* improved diabetes-induced haematological abnormalities, as evidenced by increased RBC, PCV, and haemoglobin levels, with the 600 mg/kg dose showing the greatest restorative effect. Reduced WBC and platelet counts, alongside improved erythrocyte indices, further suggest attenuation of inflammation and recovery of normal haematological function. Restoration of hemoglobin, RBC count, PCV, and normalization of WBC and platelet levels indicate reversal of diabetes-induced hematological disruptions, which often stem from oxidative stress and chronic inflammation [36]. Similar study was carried out by Teugwa et al. [29], who reported that *P. nitida* extracts exhibited restorative effect in diabetic and oxidative injury models, and attributed it to the antioxidant and membrane-stabilizing activity of flavonoids and phenolic acids. However, the mild macrocytic shift (elevated MCV and MCH) observed at higher doses suggests a compensatory erythropoietic response rather than toxicity, though this warrants further investigation through reticulocyte counts and micronutrient assays to exclude early macrocytosis are reported in [37].

During postprandial hyperglycemia, the liver is the first organ to sense the increase in circulating glucose and insulin [38]. A healthy liver responds by enhancing glycogen synthesis and suppressing gluconeogenesis, effectively limiting the rise in peripheral glucose. Liver enzyme improvements observed in treated groups, including reductions in ALT, AST, ALP, and bilirubin indicate significant hepatoprotective activity of *P. nitida*. This is consistent with the study of Onyekachukwu et al.[39], who noted significant improvement in serum protein and albumin, suggesting hepatic cellular healing and improved synthetic capacity. Previous work has similarly shown that *P. nitida* extracts mitigate hepatic insult in chemically or metabolically induced hepatotoxicity [34], likely due to radical-scavenging activity and prevention of lipid peroxidation. Phenolic compounds are widely reported for preserving hepatocyte integrity and stabilizing membrane-associated enzymes [40], which complements the pattern observed in the present findings.

CONCLUSION

The phenolic extract of *Picralima nitida* leaf demonstrated a wide safety margin, with no mortality or observable toxicity recorded even at 5000 mg/kg, indicating its practical non-toxicity. Both acute and sub-acute anti-hyperglycemic studies revealed a dose-dependent reduction in blood glucose, with the highest dose (600 mg/kg) exhibiting superior efficacy, comparable to or exceeding that of glibenclamide. Treatment with the extract also mitigated diabetes-induced body weight loss and improved hematological indices, including RBC, PCV, hemoglobin, WBC, and platelet counts, with higher doses showing more pronounced effects. Furthermore, the extract exerted

hepatoprotective effects, as evidenced by dose-dependent normalization of liver function parameters (total protein, albumin, globulin, ALT, AST, ALP, and bilirubin). Therefore, these findings indicate that the phenolic extract of *P. nitida* is safe, effectively lowers hyperglycemia, ameliorates hematological disruptions, and protects hepatic function in diabetic rats.

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AUTHORS' CONTRIBUTION

CSCE and IO conceived and designed the study. CSCE carried out the research under the supervision of IO. CSCE drafted the original manuscript and analysis, while IO reviewed and edited the manuscript. Both authors read and approved the final version of the manuscript.

CONFLICT OF INTEREST

The author declares that there are no known financial or personal conflicts of interest that could have influenced the work reported in this manuscript.

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REFERENCES

1. Siraj J, Abateka T, Kebede O. Patients' Adherence to Anti-diabetic Medications and Associated Factors in Mizan-Tepi University Teaching Hospital: A Cross-Sectional Study. Inquiry (United States) 58;2021. https://doi.org/10.1177/00469580211067477.
2. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, Cavan D, Shaw JE, Makaroff LE. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Research and Clinical Practice 128;2017:40–50. https://doi.org/10.1016/j.diabres.2017.03.024.
3. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE, Bright D, Williams R. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Research and Clinical Practice 157;2019:107843. https://doi.org/10.1016/j.diabres.2019.107843.
4. Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of Type 2 Diabetes Mellitus. International Journal of Molecular Sciences 21;2020:6275. https://doi.org/10.3390/ijms21176275.
5. Fletcher B, Gulanick M, Lamendola C. Risk Factors for Type 2 Diabetes Mellitus. Journal of Cardiovascular Nursing 16;2002:17–23. https://doi.org/10.1097/00005082-200201000-00003.
6. Safiri S, Karamzad N, Kaufman JS, Bell AW, Nejadghaderi SA, Sullman MJM, Moradi-Lakeh M, Collins G, Kolahi A-A. Prevalence, Deaths and Disability-Adjusted-Life-Years (DALYs) Due to Type 2 Diabetes and Its Attributable Risk Factors in 204 Countries and Territories, 1990–2019: Results From the Global Burden of Disease Study 2019. Frontiers in Endocrinology 13;2022. https://doi.org/10.3389/fendo.2022.838027.
7. Szalai Z, Berkó AM, Bódi N, Hermesz E, Ferencz Á, Bagyánszki M. Oxidative-Stress-Related Alterations in Metabolic Panel, Red Blood Cell Indices, and Erythrocyte Morphology in a Type 1 Diabetic Rat Model. Applied Sciences 13;2023:9920. https://doi.org/10.3390/app13179920.
8. Gupta A, Behl T, Sehgal A. Unmasking the Therapeutic Potential of Biomarkers in Type-1 Diabetes Mellitus. Biointerface Research in Applied Chemistry 11;2021:13187–13201. https://doi.org/10.33263/BRIAC115.1318713201.
9. Sundus S, Hira K, Sohail N, Habiba, Tariq A, Ara J, Sultana V, Ehteshamul-Haque S. Protective role of Pandanus tectorius Parkinson ex Du Roi in diabetes, hyperlipidemia, liver and kidney dysfunction in alloxan diabetic rats. Clinical Phytoscience 7;2021. https://doi.org/10.1186/s40816-021-00279-z.
10. Soliman HM, Wagih HM, Algaidi SA, Hafiz AH. Histological Evaluation of the Role of Atypical Antipsychotic Drugs in Inducing Non-Alcoholic Fatty Liver Disease in Adult Male Albino Rats (Light and Electron Microscopic Study). Folia Biologica (Praha) 59;2013:173–180.
11. Guerra Ruiz AR, Crespo J, López Martínez RM, Iruzubieta P, Casals Mercadal G, Lalana Garcés M,

Lavin B, Morales Ruiz M. Measurement and clinical usefulness of bilirubin in liver disease. Advances in Laboratory Medicine 2;2021:352–361. https://doi.org/10.1515/almed-2021-0047.

12. Gupta A, Behl T, Sehgal A. Unmasking the Therapeutic Potential of Biomarkers in Type-1 Diabetes Mellitus. Biointerface Research in Applied Chemistry, 11(1), 2021:13187–201. DOI: 10.33263/BRIAC115.1318713201.
13. Althaher AR, Mastinu A. Calamintha incana (Sm.) Helder: A New Phytoextract with In Vitro Antioxidant and Antidiabetic Action. Applied Sciences 13;2023:3966. https://doi.org/10.3390/app13063966.
14. Tran N, Pham B, Le L. Bioactive Compounds in Anti-Diabetic Plants: From Herbal Medicine to Modern Drug Discovery. Biology 9;2020:252. https://doi.org/10.3390/biology9090252.
15. Kabir N, Alhaji UI, James DB, Inuwa HM, Atiku MK. Effect of the combination of Leptadenia hastata (Pers.) Decne and Momordica balsamina Linn leaf extracts on lipid profile of streptozotocin-induced diabetic rats. Future Journal of Pharmaceutical Sciences 7;2021:110. https://doi.org/10.1186/s43094-021-00263-x.
16. Hu FB, Manson JE, Stampfer MJ, Colditz G, Liu S, Solomon CG, Willett WC. Diet, Lifestyle, and the Risk of Type 2 Diabetes Mellitus in Women. New England Journal of Medicine 345;2001:790–797. https://doi.org/10.1056/NEJMoa010492.
17. Butt MD, Ong SC, Rafiq A, Kalam MN, Sajjad A, Abdullah M, Malik T, Yaseen F, Babar Z-U-D. A systematic review of the economic burden of diabetes mellitus: contrasting perspectives from high and low middle-income countries. Journal of Pharmaceutical Policy and Practice 17;2024. https://doi.org/10.1080/20523211.2024.2322107.
18. Okokon JE, Antia BS, Igboasoiyi AC, Essien EE, Mbagwu HOC. Evaluation of antiplasmodial activity of ethanolic seed extract of Picralima nitida. Journal of Ethnopharmacology 111;2007:464–467. https://doi.org/10.1016/j.jep.2006.12.016.
19. Erharuyi O, Falodun A, Langer P. Medicinal uses, phytochemistry and pharmacology of Picralima nitida (Apocynaceae) in tropical diseases: A review. Asian Pacific Journal of Tropical Medicine 7(1);2014:1–8.
20. Erharuyi O, Falodun A. Free Radical Scavenging Activities of Methanol Extract and Fractions of Picralima nitida (Apocynaceae). Journal of Applied Sciences and Environmental Management 16(3);2012:291–294.
21. Shittu H, Gray A, Furman B, Young L. Glucose uptake stimulatory effect of akuammicine from Picralima nitida (Apocynaceae). Phytochemistry Letters 3;2010:53–55. https://doi.org/10.1016/j.phytol.2009.11.003.
22. Inkoto CL, Kayembe J-PK, Mpiana PT, Ngbolua K-N. A review on the phytochemistry and pharmacological properties of Picralima nitida Durand and H. (Apocynaceae family): A potential anti-COVID-19 medicinal plant species. Emergent Life Sciences Research 6;2020:64–75. https://doi.org/10.31783/elsr.2020.616475.
23. Jean Noel Yao K, Assamoi A, Antoine A, Djeneba Ouattara H, Eric Donald N'dri K. Antidiabetic activities of Picralima nitida powder, an indigenous Ivorian edible plant in type II diabetes mellitus rat model. Biomedicine and Biotechnology 8(1);2023:14–23. https://doi.org/10.12691/bb-8-1-2.
24. Mazumdar S, Marar T, Patki J, Devarajan S, Zambare V, Swami D. In silico and in vitro analysis reveal multi-target anti-hyperglycaemic properties of gedunin, a limonoid from neem (Azadirachta indica). Clinical Phytoscience 6;2020:25. https://doi.org/10.1186/s40816-020-00175-y.
25. Prince OA, Ngozi KA, Precious UE, Anthony CCE, Chinedu PN, Enyinna WC, Anthony UO, Favour JA. Phytochemical Composition, Antibacterial Activity, Proximate and Mineral Analysis of Methanol Extract from Combined Seeds and Peels of Picralima nitida. Universal Journal of Pharmaceutical Research 10(1);2025. https://doi.org/10.22270/ujpr.v10i1.1268.
26. Ufelle SA, Onyekwelu KK, Chikwendu CK. Analysis of haematological effects of Picralima nitida. Pakistan Journal of Pharmaceutical Sciences 36(4);2023:1121–1126.
27. Belhaoues S, Amri S, Bensouilah M. Major phenolic compounds, antioxidant and antibacterial activities of Anthemis praecox Link aerial parts. South African Journal of Botany 131;2020:200–205. https://doi.org/10.1016/j.sajb.2020.02.018.
28. Komalasari T, Harimurti S. A review on the anti-diabetic activity of Andrographis paniculata (Burm. f.) Nees based in-vivo study. International Journal of Public Health Science 4(4);2015:256–263.

29. Onyekachukwu EO, Osagie AM, Omage SO, Omage K, Azeke MA. Picralima nitida protects against hepatotoxicity and oxidative stress in alloxan-induced diabetic rats. Comparative Clinical Pathology, 30(1), 2021:981–93. DOI: 10.1007/s00580-021-03297-y.
30. Chinedu E, Arome D, Ameh F. A new method for determining acute toxicity in animal models. Toxicology International 20(3);2013:224–226. https://doi.org/10.4103/0971-6580.121674.
31. Chidiebere Ikaraoha I, Nnodim J. The Effects of Ethanol Extract from the Seeds, Leaves and Barks of Picralima Nitida on the Platelet Indices in Albino Rats. Journal of Medical Discoveries, 2024;1-10 https://doi.org/rpc/2024/jmd/0006
32. Uthman, T. O., Oloyede, O. B., Owolarafe, T. A., Yakubu, M. T., & Dosumu, O. O. Toxicopathological evaluation of Picralima nitida seed aqueous extract in Wistar rats. Turkish Journal of Biochemistry, 39 (2); 2014;119–125. doi: 10.5505/tjb.2014.83997
33. Kwon H, Park B. Borderline-high mean corpuscular volume levels are associated with arterial stiffness among the apparently healthy Korean individuals. Korean Journal of Family Medicine 41(6);2020:387–391. https://doi.org/10.4082/kjfm.19.0061.
34. Lages M, Barros R, Moreira P, Guarino MP. Metabolic effects of an oral glucose tolerance test compared to the mixed meal tolerance tests: A narrative review. Nutrients 14(10);2022:2032. https://doi.org/10.3390/nu14102032.
35. De Campos OC, Osaigbovo DI, Bisi-Adeniyi TI, Iheagwam FN, Rotimi SO, Chinedu SN. Protective role of Picralima nitida seed extract in high-fat high-fructose-fed rats. Advances in Pharmacological and Pharmaceutical Sciences 2020;2020:1–11. https://doi.org/10.1155/2020/5206204.
36. Naz D, Muhamad A, Zeb A, Shah I. In vitro and in vivo antidiabetic properties of phenolic antioxidants from Sedum adenotrichum. Frontiers in Nutrition 6;2019. https://doi.org/10.3389/fnut.2019.00177.
37. Bashiru SO, Olatunde OF. Hyperglycaemic environment: Contribution to the anaemia associated with diabetes mellitus in rats experimentally induced with alloxan. Anemia 2015;2015:1–6. https://doi.org/10.1155/2015/848921.
38. Mansour A, Mousa M, Abdelmannan D, Tay G, Hassoun A, Alsafar H. Microvascular and macrovascular complications of type 2 diabetes mellitus: Exome wide association analyses. Frontiers in Endocrinology 14;2023. https://doi.org/10.3389/fendo.2023.1143067.
39. Dimitriadis GD, Maratou E, Kountouri A, Board M, Lambadiari V. Regulation of postabsorptive and postprandial glucose metabolism by insulin-dependent and insulin-independent mechanisms: An integrative approach. Nutrients 13(1);2021. https://doi.org/10.3390/nu13010159.
40. Onyekachukwu EO, Osagie AM, Omage SO, Omage K, Azeke MA. Picralima nitida protects against hepatotoxicity and oxidative stress in alloxan-induced diabetic rats. Comparative Clinical Pathology 30;2021:981–993. https://doi.org/10.1007/s00580-021-03297-y.
41. Ma X, Xiong S, Xiang F, Li Y, Lin Y, Liu Y, Lin L, Xie J. The protective effect of phenolic acids on liver disease: A review of possible mechanisms. Antioxidants 14(10);2025:1247. https://doi.org/10.3390/antiox14101247.