

## HYPOGLYCAEMIC POTENTIAL OF AQUEOUS EXTRACTS OF *Moringa oleifera* LEAVES AND *Tamarindus indica* FRUITS ON STREPTOZOTOCIN-INDUCED DIABETIC ALBINO RATS

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### ABSTRACT

Diabetes mellitus is a common, albeit potentially devastating medical condition whose management primarily includes lifestyle modifications and pharmacological interventions. However, these conventional treatments often have limitations such as undesirable side effects, high costs, and limited accessibility, especially in developing countries. Hence, there has been a growing interest in exploring alternative therapies, including the use of medicinal plants with potential hypoglycaemic properties. The study investigated the hypoglycaemic effects of aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on diabetic rats. Thirty-five rats were divided into seven groups, including controls, standard treatment with glybenclamide, and various combinations of plant extracts- normal control group (NC) received placebo, 0.5 ml DMSO, STZ and positive control groups received 60 mg/kg b.w STZ and 80 mg/kg b.w glybenclamide respectively. The other four groups received respectively *M. oleifera* (500 mg/kg b.w), *T. indica* (500 mg/kg b.w), *M. oleifera* and *T. indica* (500 mg/kg b.w each), *M. oleifera* and *T. indica* (250 mg/kg b.w each). The extracts contained phytochemicals such as ferulic acid, tannic acids, caffeine, salicylic acid, theophylline, and coumaric acid. Results showed that diabetic rats experienced weight loss and increased blood glucose levels, but treatment with the plant extracts and standard drug significantly improved these parameters. The findings suggested that these plant extracts may have potential as alternative therapies for diabetes management and its complications.

**Keywords:** Diabetes, hypoglycaemia, streptozotocin, *Moringa*, *Tamarindus*

### INTRODUCTION

Diabetes is a serious, chronic, and complex metabolic disorder of multiple aetiologies with profound consequences, both acute and chronic (Mishra *et al*, 2024). It is a global endemic disease with rapidly increasing prevalence in both developing and developed countries (Namazi *et al*, 2024). The pathophysiology of diabetes mellitus involves complex interactions between genetic and environmental factors (Ogrotis *et al*, 2023). Type 2 diabetes, which is more common, involves insulin resistance and relative insulin

deficiency (Lema-Pérez, 2021). It is directly linked to obesity and accounts for 80% of cases (Pradeepa and Mohan, 2021). Chronic hyperglycaemia in diabetes leads to oxidative stress, which plays a crucial role in the development of complications (Bhatti *et al*, 2022). The economic burden of diabetes is also substantial, given the costs associated with medical care, loss of productivity, and long-term disability (Banker *et al.*, 2021). According to recent demographic data, an estimated 451 million adults worldwide were diagnosed with diabetes in 2017 alone, with a projected increase to 693 million by 2045 if current trends continue and appropriate management and prevention techniques are not developed (Nwanna *et al*, 2024).

Patients with diabetes who have had the disease for a long time develop a number of comorbidities (Guzzi *et al*, 2023). It usually starts with macrovascular problems, then progresses to cardiovascular disease and stroke, increased cardiovascular morbidity, and, eventually, mortality. Furthermore, nephropathy, retinopathy, and neuropathy are all possible outcomes of these macrovascular problems (Nwanna *et al*, 2024).

The management of diabetes primarily includes lifestyle modifications and pharmacological interventions (Borse *et al*, 2021). However, these conventional treatments often have limitations such as side undesirable effects, high costs, and limited accessibility, especially in developing countries (Jugran *et al*, 2021). Consequently, there is a growing interest in exploring alternative therapies, including the use of medicinal plants with potential hypoglycaemic properties.

Medicinal plants, such as *Moringa oleifera* and *Tamarindus indica*, have been used in traditional medicine for centuries to treat ailments like diabetes (Mohanta *et al*, 2023; Süntar, 2020). They are particularly popular in developing countries due to their accessibility, affordability, and cultural acceptability (Jikah and Edo, 2023; Olanipekun, 2023). *Moringa oleifera*, commonly known as the drumstick tree is native to parts of Africa and Asia (Tende *et al*, 2011). It is a highly valued plant for its nutritional and medicinal properties (Klimek-Szczykutowicz *et al*, 2024). Studies have reported the potential health benefits of *Moringa oleifera*, including its hypoglycaemic effects (Hamza *et al*, 2023). *Tamarindus indica*, commonly known as tamarind is a tropical fruit-bearing tree widely distributed in Africa, India, and other tropical regions (Lorence *et al*, 2023). The fruit pulp and seeds are rich in various nutrients and phytochemicals, including flavonoids, polyphenols, and tannins (Mukherjee *et al*, 2024). Studies have highlighted the potential of *Tamarindus indica* in managing diabetes and related complications (Kathirvel *et al*, 2024). The hypoglycaemic effects of tamarind have been linked to its ability to enhance insulin secretion, improve glucose uptake, and modulate carbohydrate metabolism (Nwanna *et al*, 2024).

The present study therefore, investigated the hypoglycaemic potential of aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on streptozotocin- induced diabetic albino rats.

## **MATERIALS AND METHOD**

### **Collection of Plant Materials**

Fresh but matured leaves of *Moringa oleifera* and *Tamarindus indica* fruit samples were harvested from the Agriculture Research Farm, Federal University Wukari. The plant

samples were identified and authenticated at the Department of Biological Sciences, Federal University Wukari. The leaves and fruits were rinsed severally with clean tap water to remove dust particles and debris and thereafter allowed to dry completely in preparation for extraction.

### **Preparation of plant extracts**

Aqueous extract of *T. indica* pulps were extracted according to the method described by Tekou *et al* (2023). An equivalent of 10 g of macerated fruit pulp samples was measured into 100 mL of water in a conical flask and allowed to stand for 24 hours with gentle stirring. The mixtures were afterwards filtered using a Whatman Grade 1 filter paper (Cytiva, MA). The resulting filtrates were dried at 45 °C in an air oven to obtain the aqueous extract. The percentage yield was calculated using Equation 1. The extracts were stored in the freezer at -4°C for later use.

$$Yield (\%) = \frac{Mass\ of\ Extract}{Mass\ of\ Powder} \times 100$$

### **Equation 1**

Aqueous extract of *M. oleifera* leaves were extracted according to the method described by Tuorkey (2016). *Moringa* aqueous extracts were prepared by mixing 10 g of dried and powdered *M. oleifera* leaves with 100 mL of distilled water for 24 h and then stored at 4 °C. Afterward, the mixtures were filtered twice through a 2 µm pore filter paper. The aqueous extract stock solutions (100 mg/mL) were stored at 4 °C for up to 5 days and freshly prepared for each set of experiment.

### **Determination of the phytochemical composition of plants extracts**

The plants extracts were screened for the presence of various phytoconstituents like alkaloids, flavonoids, phenolics, steroids, tannins, glycosides, triterpenoids, and saponins in accordance with the Association of Official Analytical Chemists (AOAC) methods (Tekou *et al*, 2023).

### **Determination of total phenolic content of extracts**

The total phenolic content was determined using the Folin-Ciocalteu method as described by Kuddus *et al* (2020). Leaf extract (100  $\mu$ L), 500  $\mu$ L of Folin-Ciocalteu reagent and 400  $\mu$ L of 7.5% sodium bicarbonate were mixed together, and the resulting mixture was incubated at 40 °C for 20 min. Absorbance was taken at 755 nm using a spectrophotometer against a blank and total phenol content calculated in mg/g using a standard curve of gallic acid.

### **Determination of the total flavonoid content**

The total flavonoid content of the extracts was quantified using the aluminium chloride colorimetric assay for quantitative determination as described by Fagbemi *et al* (2022). Briefly, 1 mL of the extract was added to 2.8 mL of distilled water and mixed with 0.1 mL of 1 mg/mL potassium acetate solution. Then, 0.1 mL of 10% aluminium chloride ( $\text{AlCl}_3$ ) was added to this solution. After 30 min of incubation, the absorbance was monitored and measured at 415 nm by using a UV-visible spectrophotometer. Total flavonoid content was expressed as gallic acid equivalents (GAE) in milligram/gram dry weight.

### **Determination of alkaloids contents**

An equivalent of 10 mg of the plant extract was weighed and dissolved in 10 mL of 2 N HCl and filtered utilizing Whatman no.1 filter paper. Then 1 mL of the acidic extract (1 mg/mL) was transferred to a separating funnel and the solution was washed with chloroform (10 mL  $\times$  3 times) to remove non-alkaloidal materials. The pH was adjusted to neutral using 0.1 N NaOH. Then, 5 mL of BCG solution and 5 mL of phosphate buffer (pH 4.7) were added to the neutral solution and mixed well. The yellow-coloured complex was extracted with chloroform (1, 2, 3, and 4 mL) by vigorous shaking. The chloroform extracts were extracted in a 10 mL volumetric flask. The absorbance of the chloroform layer was measured with a spectrophotometer at 470 nm against a chloroform blank. The total alkaloid content was calculated from the standard curve and expressed as mg/100 g of plant material (Van, 2018).

### **Determination of Tannins**

A 0.5 g aliquot of the sample was added into 50 mL of distilled water and agitated on a shaker for 1 hr at 230 rpm. Subsequently, the samples were filtered utilizing Whatman no.1 filter paper, and 2 mL of the tannin's reagent (comprising 0.1 M  $\text{FeCl}_3$  in 0.1 N HCl and 0.008 M potassium ferrocyanide) was added to 5 mL of the filtrate (Hossain, 2020). The spectrophotometric measurement of absorbance at 605 nm was conducted within 5 minutes using a spectrophotometer. Tannin content was determined using a standard curve, involving dilutions ranging from 10-50 mg/5 mL of tannic acid (Wilhelmy *et al*, 2021).

### **Acute toxicity test**

The acute toxicity and lethality test of the aqueous plant extracts in rats was estimated using the method of Lorke as described by Ayobami *et al* (2020) and the animals were observed continuously after every 2 hrs for the following profiles: Behavioural Profile- Alertness, restlessness; Neurological Profile- Pain response, touch response, gait; Autonomic Profile- Defecation and urination. Finally, after a period of 24 hrs., the animals were observed for any lethality or death.

### **Experimental animal**

Thirty-five healthy 12-months old male albino rats of between 150 g and 200 g were purchased. They were kept for two weeks to acclimatize with the environment in clean cages (zinc plate bottom and wire mesh top) and maintained under standard laboratory conditions (Temperature  $25 \pm 5^{\circ}\text{C}$ , Relative humidity 50% to 60%, and a 12/12 h light/dark cycle) and were fed with standard diet and water *ad libitum*. Any rat that weighed above 250 g after 2 weeks was considered obese. All the procedures were in accordance with the protocol of National Animal Care and Use Committee and Guidelines for the Care and Use of Experimental Animals (Díaz *et al*, 2021).

### **Experimental induction of diabetes**

Diabetes was induced in the rats according to the method described by Tekou *et al* (2023). A single dose of 45 mg/kg b.w streptozotocin (STZ) was administered to the animals by an intraperitoneal route. Hyperglycaemia was confirmed after 3 days and rats with blood glucose level of  $\geq 200$  mg/dL were considered diabetic and treated with the plant extracts for twenty-eight (28) days.

### **Experimental design and administering of plant extracts**

Thirty-five rats randomly divided into seven different experimental groups of 5 animals each. Three control groups were used, normal control group (NC) received placebo, 0.5 ml DMSO, STZ- control and positive control group (PC) received glybenclamide (80 mg/kg b.w) (Ayobami *et al*, 2020); the other four groups received respectively *Moringa oleifera* (500 mg/kg b.w), *Tamarindus indica* (500 mg/kg b.w), *Moringa oleifera* and *Tamarindus indica* (500 mg/kg b.w each), *Moringa oleifera* and *Tamarindus indica* (250 mg/kg b.w each) (Tekou *et al*, 2023). The plant extracts were administered orally using oral gavages for a duration of 28 days after induction of diabetes.

**Group 1:** rats administered placebo, 0.5 mL DMSO

**Group 2:** rats administered 60 mg/kg b.w STZ control

**Group 3:** rats administered glybenclamide (80 mg/kg b.w)

**Group 4:** rats administered 500 mg/kg b.w *Moringa oleifera*

**Group 5:** rats administered 500 mg/kg b.w *Tamarindus indica*

**Group 6:** rats administered 500 mg/kg b.w *Moringa oleifera* and *Tamarindus indica* (500 mg/kg b.w)

**Group 7:** rats administered 250 mg/kg b.w *Moringa oleifera* and *Tamarindus indica* (250 mg/kg b.w)

### Animal sacrifice

At the end of the experimental period, the animals were fasted for 12 h, then anaesthetized using ketamine (administered by the intraperitoneal route at 10 mg/kg b.w) and dissected. The dissecting instruments were washed with 5% nitric acid and rinsed several times with distilled water before use. Whole blood was obtained by cardiac puncture into sterile plain tubes for the haematological assays (Ayobami *et al*, 2020).

### Evaluation of blood glucose level

The blood glucose level (expressed in mg/dL) were measured using 5-10  $\mu$ L of blood obtained from the tail tip cut after overnight fasting (8 hr) using a portable glucometer (Accu-Check) every five days during the treatment (Tekou *et al*, 2023).

### Haematological assessment

The levels of selected haematological indices including, red blood cells (RBC), haemoglobin (Hb), packed cell volume (PCV), white blood cell (WBC) were determined using automated haematological analyser (Hajam *et al*, 2020; Ali and Hassan, 2019).

### Data Analysis

Data generated were analysed using one-way ANOVA followed by Duncan multiple comparison test to determine the significance of differences between groups with the use of statistical package for social sciences (SPSS) version 23. The data obtained were expressed as mean  $\pm$  standard deviation (SD), where values will be considered statistically significant at  $p < 0.05$ .

## RESULTS AND DISCUSSION

### RESULTS

Phytochemical Contents of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits Evaluated by High Performance Liquid Chromatography (HPLC)

The phytochemical contents of aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits were quantified by HPLC. Tables 1 and 2 provide a summary of the chromatographs of both extracts. Ferulic acid, tannic acids, caffeine, salicylic acid and theophylline were present in aqueous extract of *Moringa oleifera* with tannic (14.3 mg) and salicylic acids (14.2 mg) predominating. On the other hand, Coumaric acid (25.49 mg) was predominant in the aqueous extracts of *Tamarindus indica* fruits whereas tannic acid (3.3 mg) was found to be lower compared to other compounds.

**Table 1 Amounts and Percentages of Phytochemicals Present in Aqueous Extracts of *Moringa oleifera* Leaves**

SN	Retention time (min)	Amount (mg)	Amount (%)	Compound
1	0.317	0.484	0.8	
2	3.897	29.447	51.3	
3	4.410	6.582	11.5	Ferulic Acid
4	5.825	8.213	14.3	Tannic Acid
5	6.275	1.407	2.5	Caffeine
6	6.823	8.166	14.2	Salicylic Acid
7	7.948	3.052	5.3	Theophylline
	Total	57.351	100.0	

**Table 2 Amounts and Percentages of Phytochemicals Present in Aqueous Extracts of *Tamarindus indica* fruits**

SN	Retention time (min)	Amount (mg)	Amount (%)	Compound
1	0.405	20.022	25.4	Coumaric Acid
2	2.380	25.494	32.3	
3	2.598	3.435	4.4	Phenol
4	3.945	18.271	23.2	Ferulic Acid
5	4.493	8.996	11.4	
6	5.880	2.594	3.3	Tannic Acid
	Total	78.8111	100.0	

**Effects of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Body Weight of STZ-induced Diabetic Albino Rats**

The mean body weights of all the rats were noted before STZ induction (Week 0 of diabetes) and at the end of the various treatments at Week 3 (Figure 1). The weekly mean body weights (WMBW) of the rats in week 0 across the experimental groups did not show significant ( $p > 0.05$ ) increase as compared to the normal control (Group 1). However, there was decrease in the weekly mean body weights in the STZ-induced groups in week 3 as compared to the normal control (Group 1). On the other hand, the extracts and standard drug- treated groups (3, 4, 5, 6 and 7) showed significant increase in the body weights most especially in week 3 when compared with the STZ-controlled group (Group 2).

**3.1.4 Effects of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Weekly Mean Blood Glucose Levels (WMBGL) of STZ-induced Diabetic Albino Rats**

The mean blood glucose levels of all the rat groups were noted before STZ administration and at the end of the various treatments in Week 3 (Figure 2). The WMBGL of the rats in week 0 (week before induction of diabetes) across the experimental groups did not display significant ( $p > 0.05$ ) increase as compared to the normal control (Group 1). However, there was increase in the WMBGL in the STZ-induced groups in week 1 as compared to the normal control (Group 1). Consequently, the extracts and standard drug- treated groups (3, 4, 5, 6 and 7) showed appreciable reduction in the blood glucose levels in week 2, and most especially in week 3 when compared with the STZ-controlled group (Group 2).

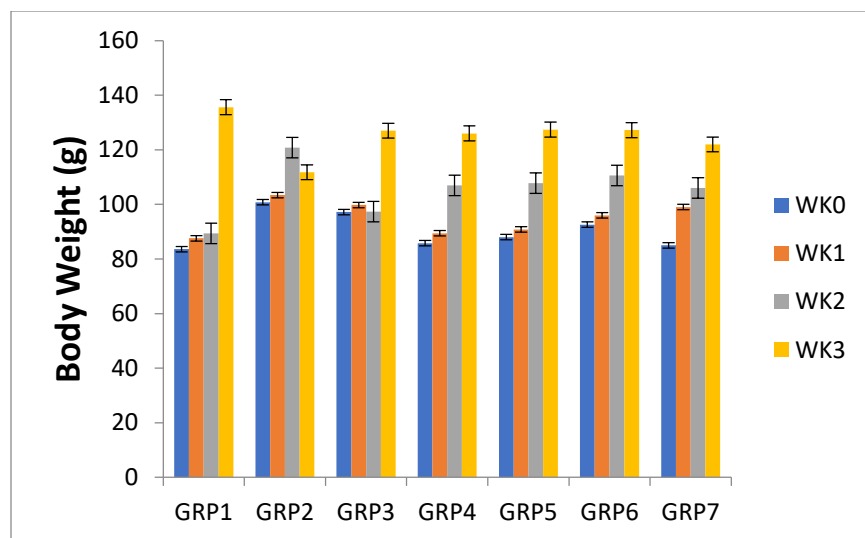


Figure 1 Effect of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Weekly Body Weight of STZ-induced Diabetic Albino Rats

GRP1 = Normal control; GRP2 = STZ-Control; GRP3 = 100 mg/kg Gliclazide; GPR4 = 500 mg/kg Moringa Extract; GRP5 = 500 mg/kg Tamarin Extract; GRP6 = 500 mg/kg each Moringa and Tamarin Extracts; GRP7 = 250 mg/kg each Moringa and Tamarin Extracts.

### **Effects of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Haematological Parameters of STZ-induced Diabetic Rats**

The red blood cells (RBC), haemoglobin concentration (Hb), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red blood distribution-coefficient of variation (RDW-CV) and red blood distribution-standard deviation (RDW-SD) of the STZ- control (Group 2) were significantly ( $p < 0.05$ ) decreased when compared with normal control rats (Table 3). However, treatment of diabetic rats with the aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits caused significant ( $p < 0.05$ ) increase in the aforementioned parameters.

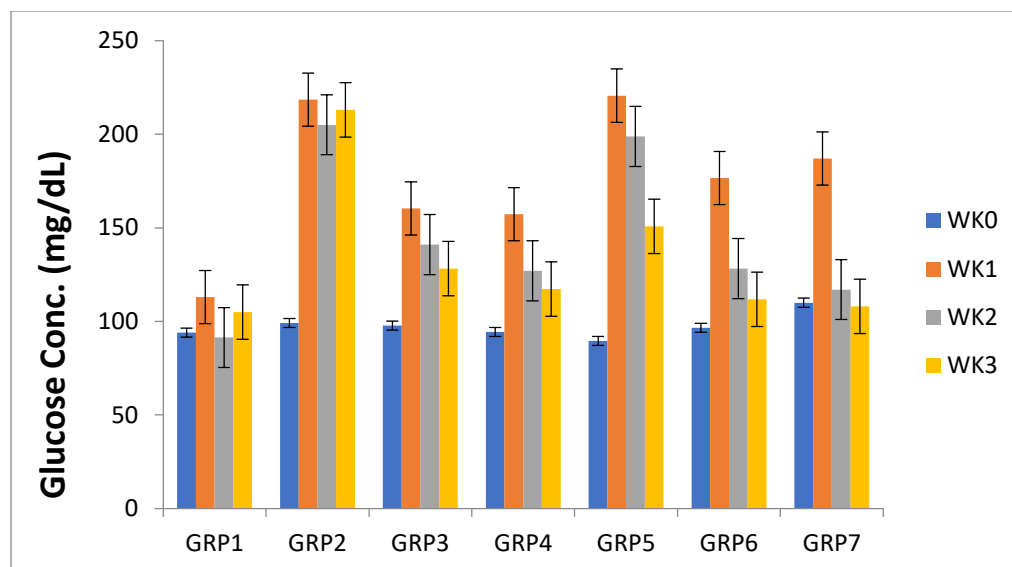


Figure 2 Effect of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Weekly Glucose Levels of STZ-induced Diabetic Wistar Rats.

GRP1 = Normal control; GRP2 = STZ-Control; GRP3 = 100 mg/kg Gliclazide; GPR4 = 500 mg/kg Moringa Extract; GRP5 = 500 mg/kg Tamarin Extract; GRP6 = 500 mg/kg each Moringa and Tamarin Extracts; GRP7 = 250 mg/kg each Moringa and Tamarin Extracts

Table 4 summarizes the observed changes in WBC differential indices with the different experimental treatments. WBC count, lymphocyte count and percentages were increased significantly ( $p < 0.05$ ) in the diabetic control rats compared to the normal control. However, following treatments with aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits, the total white cell count (WBC), lymphocyte count and percentages were decreased significantly ( $p < 0.05$ ) compared with the normal control. On the other hand, (Monocytes, eosinophils and basophils (MID) cells and granulocytes were significantly ( $p < 0.05$ ) increased in the diabetic treated groups when compared with the STZ-control.

Platelet indices were increased in diabetic rats compared to normal control, but were decreased upon treatment with the plant preparations (Table 5).

**Table 3 Effect of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Red Blood Cells Differential of STZ-induced Diabetic Wistar Rats**

Group	RBC ( $10^{12}/L$ )	HGB (g/L)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/L)	RDW-CV (%)	RDW-SD (fL)
GRP1	4.3±0.40 <sup>a</sup>	10±1.64 <sup>a</sup>	26.05±3.78 <sup>a</sup>	60.35±3.23 <sup>a</sup>	23.25±1.70 <sup>a</sup>	385±6.57 <sup>a</sup>	15.35±0.60 <sup>a</sup>	34.9±2.30 <sup>a</sup>
GRP2	1.75±0.28 <sup>b</sup>	4±0.96 <sup>b</sup>	9.95±7.94 <sup>b</sup>	41±0.33 <sup>a</sup>	14.2±0.44 <sup>b</sup>	297±8.76 <sup>b</sup>	8.1±0.00 <sup>b</sup>	27.1±0.11 <sup>b</sup>
GRP3	4.89±0.17 <sup>a</sup>	9.6±0.92 <sup>a</sup>	24.85±1.06 <sup>a</sup>	58.4±0.00 <sup>a</sup>	22.55±0.49 <sup>a</sup>	386±7.67 <sup>a</sup>	15.3±0.77 <sup>a</sup>	34.45±1.92 <sup>a</sup>
GRP4	4.01±0.03 <sup>a</sup>	9.1±0.11 <sup>a</sup>	23.75±0.60 <sup>a</sup>	59.3±1.97 <sup>a</sup>	22.75±0.38 <sup>a</sup>	384±5.48 <sup>a</sup>	14.85±0.82 <sup>a</sup>	34±3.07 <sup>a</sup>
GRP5	3.53±0.19 <sup>a</sup>	7.7±1.10 <sup>a</sup>	20.2±3.83 <sup>a</sup>	57.1±1.31 <sup>a</sup>	21.95±0.49 <sup>a</sup>	385±17.53 <sup>a</sup>	13.95±0.82 <sup>a</sup>	30.6±1.75 <sup>a</sup>
GRP6	4.07±0.06 <sup>a</sup>	8.2±0.77 <sup>a</sup>	23.5±0.88 <sup>a</sup>	57.75±1.26 <sup>a</sup>	20.05±1.59 <sup>a</sup>	347.5±20.27 <sup>a</sup>	15.05±0.49 <sup>a</sup>	32.95±2.57 <sup>a</sup>
GRP7	3.17±0.09 <sup>a</sup>	7.8±0.11 <sup>a</sup>	21.65±0.49 <sup>a</sup>	57.33±1.78 <sup>a</sup>	19.96±1.73 <sup>a</sup>	346.5±17.77 <sup>a</sup>	14.09±0.11 <sup>a</sup>	30.83±2.44 <sup>a</sup>

Values are expressed as mean ± S.D (n = 7). Mean with similar superscript on the same column are not significantly different (P < 0.05). RBC: red blood cell, Hb: haemoglobin, Hct: Haematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular haemoglobin, MCHC: mean corpuscular haemoglobin concentration, RDW-CV: red cell distribution width - coefficient of variation RDW-SD: red cell distribution width-standard deviation.

GRP1 = Normal control; GRP2 = STZ-Control; GRP3 = 100 mg/kg Gliclazide; GPR4 = 500 mg/kg Moringa Extract; GRP5 = 500 mg/kg Tamarin Extract; GRP6 = 500 mg/kg each Moringa and Tamarin Extracts; GRP7 = 250 mg/kg each Moringa and Tamarin Extracts

**Table 4 Effect of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on White Blood Cells Differential of STZ-induced Diabetic Wistar Rats**

Group	WBC (10 <sup>9</sup> /L)	LYM (10 <sup>9</sup> /L)	MID (10 <sup>9</sup> /L)	GRAN (10 <sup>9</sup> /L)	LYM (%)	MID (%)	GRAN (%)
GRP1	11.85±3.01 <sup>a</sup>	10.55±3.01 <sup>a</sup>	0.75±0.05 <sup>a</sup>	0.55±0.05 <sup>a</sup>	88.85±.57 <sup>a</sup>	6.35±1.26 <sup>a</sup>	4.8±0.40 <sup>a</sup>
GRP2	18.7±0.14 <sup>b</sup>	22.35±1.40 <sup>b</sup>	0.15±0.11 <sup>b</sup>	0.15±0.05 <sup>b</sup>	110.45±2.90 <sup>b</sup>	1.3±0.77 <sup>b</sup>	1.25±1.28 <sup>b</sup>
GRP3	9.95±3.45 <sup>a</sup>	9.1±3.40 <sup>a</sup>	0.5±0.16 <sup>a</sup>	0.2±0.11 <sup>b</sup>	89.8±0.88 <sup>a</sup>	5.4±0.22 <sup>a</sup>	4.8±2.57 <sup>a</sup>
GRP4	8.25±1.92 <sup>a</sup>	7.35±1.81 <sup>a</sup>	0.6±0.11 <sup>a</sup>	0.3±0.00 <sup>b</sup>	88.45±1.70 <sup>a</sup>	7.4±0.77 <sup>a</sup>	4.15±0.03 <sup>a</sup>
GRP5	13.2±4.05 <sup>a</sup>	11.5±2.60 <sup>a</sup>	1.1±0.22 <sup>c</sup>	0.6±0.33 <sup>a</sup>	84.65±8.71 <sup>a</sup>	9.45±4.55 <sup>a</sup>	5.9±0.59 <sup>a</sup>
GRP6	12.65±1.85 <sup>a</sup>	10.55±2.64 <sup>a</sup>	1.2±0.77 <sup>c</sup>	0.9±0.44 <sup>c</sup>	83.75±0.82 <sup>a</sup>	9.1±1.10 <sup>a</sup>	7.15±0.06 <sup>a</sup>
GRP7	10.11±1.45 <sup>a</sup>	8.15±1.67 <sup>a</sup>	0.7±0.07 <sup>a</sup>	0.5±0.11 <sup>a</sup>	82.75±0.12 <sup>a</sup>	6.1±0.10 <sup>a</sup>	6.35±0.02 <sup>a</sup>

Values are expressed as mean ± S.D (n = 7). Mean with similar superscript on the same column are not significantly different (P < 0.05). WBC: white blood cell; Lymh: lymphocytes; Mid: mid cells; Gran: granulocytes.

GRP1 = Normal control; GRP2 = STZ-Control; GRP3 = 100 mg/kg Gliclazide; GPR4 = 500 mg/kg Moringa Extract; GRP5 = 500 mg/kg Tamarin Extract; GRP6 = 500 mg/kg each Moringa and Tamarin Extracts; GRP7 = 250 mg/kg each Moringa and Tamarin Extracts

**Table 5 Effect of Aqueous Extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on Platelet Differential of STZ-induced Diabetic Wistar Rats**

GROUP	PLT	MPV	PDW	PCT	P-LCC	P-LCR
GRP1	112±17.99 <sup>a</sup>	7.95±0.82 <sup>a</sup>	16.25±1.26 <sup>a</sup>	0.342±0.21 <sup>a</sup>	13±4.82 <sup>a</sup>	13.8±3.29 <sup>a</sup>
GRP2	577±151.17 <sup>b</sup>	19.5±0.11 <sup>b</sup>	28.55±0.27 <sup>b</sup>	5.4535±0.14 <sup>b</sup>	96.5±11.22 <sup>b</sup>	27.2±0.11 <sup>b</sup>
GRP3	132±0.00 <sup>c</sup>	11±0.00 <sup>c</sup>	17.4±0.00 <sup>a</sup>	0.584±0.00 <sup>a</sup>	14±0.00 <sup>a</sup>	17±0.00 <sup>a</sup>
GRP4	118.5±12.99 <sup>a</sup>	6.7±0.66 <sup>a</sup>	14.95±0.38 <sup>a</sup>	0.83±0.05 <sup>c</sup>	13±5.86 <sup>a</sup>	14.25±3.78 <sup>a</sup>
GRP5	144±15.34 <sup>c</sup>	7.35±0.27 <sup>a</sup>	15.2±0.11 <sup>a</sup>	0.7065±0.02 <sup>c</sup>	16.5±2.74 <sup>a</sup>	11.45±0.49 <sup>a</sup>

GRP6	303.5±15.2 <sup>d</sup>	8.1±0.77 <sup>a</sup>	15.05±0.49 <sup>a</sup>	0.8585±0.20 <sup>c</sup>	15.5±4.75 <sup>a</sup>	15.05±5.42 <sup>a</sup>
GRP7	311.1±15.21 <sup>d</sup>	7.2±0.61 <sup>a</sup>	16.02±0.12 <sup>a</sup>	0.8585±0.10 <sup>c</sup>	16.4±4.15 <sup>a</sup>	15.45±4.31 <sup>a</sup>

Values are expressed as mean ± S.D (n = 7). Mean with similar superscript on the same column are not significantly different (P < 0.05).

GRP1 = Normal control; GRP2 = STZ-Control; GRP3 = 100 mg/kg Gliclazide; GPR4 = 500 mg/kg Moringa Extract; GRP5 = 500 mg/kg Tamarin Extract; GRP6 = 500 mg/kg each Moringa and Tamarin Extracts; GRP7 = 250 mg/kg each Moringa and Tamarin Extracts

## DISCUSSION

The undesirable side effects of synthetic drugs provide an incentive to modern medicine search for superior alternatives for the treatment of metabolic diseases. Herbal medicine turned out to be a hopeful therapy for the effective treatment of diabetes in the foreseeable future (Okur *et al*, 2017). In this context, the present study essentially evaluated the ameliorative effects of aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits on STZ-induced diabetic rats.

Numerous studies have suggested that phytochemicals are potentially the bioactive compounds in plants that hold promise to combat the onset and progression of oxidative stress, chronic diseases and aging. Cicero and Colletti (2016) reported that nutraceuticals of plant origin could be the possible therapeutic tool to treat the metabolic syndrome. The report also listed out the phytochemicals and their impact on diabetes and its related complications. In view of the importance of phytochemicals in providing amelioration to different ailments, the preliminary phytochemical analysis was carried out for phenols in both aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits. Among the phytochemicals, phenols and flavonoids are the most important phytochemicals which possess antibacterial, anti-inflammatory, antidiabetic, anti-cancer and antioxidant properties (Patel *et al*, 2011). Hence, total phenols and flavonoids were quantified in the aqueous extracts under *in vitro* conditions. Phenolic compounds, for instance phenolic acids and flavonoids, could promote health benefits by reducing the risk of metabolic syndrome and the related complications of type 2 diabetes. However, different groups of phenolic compounds have different biological characteristics, and very little is known about the mechanisms by which they could contribute to the prevention of the disease; there still is the need for further studies (Lin *et al*, 2016).

Diabetes is a condition of hyperglycaemic state with general symptoms including weight loss, increase thirst, hunger, and complications like diabetic nephropathy, retinopathy and fatty liver disease. In the present study, diabetes was induced in albino rats through intraperitoneal injection of STZ at a dose 75 mg/kg b. w. STZ is a chemical widely used for induction of diabetes in animal models (Lenzen, 2008). In the present study, the ameliorative effects of *Moringa oleifera* and *Tamarindus indica* extracts were studied in STZ-induced diabetic albino rats. The mean body weight and blood glucose levels of all the rats were noted on week 0 of experiment. However, a more significant decrease (p < 0.05) in the mean body weight of the STZ-control group was observed compared with the extract- treated groups. This was similar to the reduction in the body weight of diabetic animals observed by Oyedemi *et al* (2021). This decrease in body weight in STZ- induced

diabetic animals was probably due to degradation of structural proteins and muscle wasting as also espoused by Oyedemi *et al.* (2021). Streptozotocin- induced diabetic control rats may have experienced more polyuria, polyphagia and polydipsia suggesting that the rats suffered from excess fatigue eventually resulting in the weight loss when compared to normal and treated rats. At the end of experiment, the diabetic rats treated with aqueous extract of *Moringa oleifera* leaves and *Tamarindus indica* fruits gained some weight. Their body weights were significantly higher when compared with the diabetic control rat group 2. The increase in body weights of the animals was also observed in standard drug- treated rats, which implied the blood glucose stabilization effect that prevented loss of body weights (Soni *et al.*, 2018).

The blood glucose levels of all the diabetic rat groups were significantly increased ( $p < 0.05$ ) when compared with the normal control rat group on week 2. Streptozotocin administration causes the suppression of insulin and consequently abnormally elevated blood glucose level (Yin *et al.*, 2006). The type of diabetes induced during this study was type 1 as it was induced by injection of a single dose of STZ. It has been reported that injection of single dose of STZ causes Type 1 diabetes in rodents (Yin *et al.*, 2006). Type 2 diabetes can be induced by STZ injection after administration of nicotinamide. Consequently, a decrease in the MBGL of diabetic rat in groups treated with aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits was observed in all the experimental test groups. The blood glucose level of those rats was significantly ( $p < 0.05$ ) lower when compared with the untreated diabetic control rat group 2. The improvement in body weight and decrease in the blood glucose level of diabetic rats treated with the extracts indicated their hypoglycaemic effects. This antidiabetic effect of these plant extracts may be due to insulin- like effect of phytochemical ingredients contained in the extracts or increase in insulin secretion from the pancreatic islets  $\beta$ -cells following exposure to phytochemical ingredients. The findings were in agreement with the report of Jaiswal *et al.* (2017) where phytochemicals were implicated in the anti-diabetic activity of extracts of *Anacardium occidentale* leaves on streptozotocin diabetic rats.

Haematological parameters give information on the physiological states of blood cells, and these parameters may suffer distortions in diabetic rats. In this study, the indices (RBC, WBC and platelets) were altered in the diabetic rats as compared to normal rats, a finding that was inconsonance with the ones by earlier researchers (Essiet *et al.*, 2020; Adeyi *et al.*, 2021; Ezeigwe *et al.*, 2023). RBCs indices are used to evaluate erythropoiesis or lack of it. Alterations in the process may be in the direction of a decrease, indicated by anaemia or an increase, indicated by polycythaemia. The observed decrease in RBCs and related indices (Hb, PCV, MCV, MCH and MCHC) in the diabetic rats compared to the normal group thus suggested anaemia, consistent with previous report of Udoh *et al.* (2013). The decrease in the RBCs probably resulted from the excess ROS generated by the streptozotocin, causing structural alterations to their membranes (Gwozdziński *et al.*, 2021). However, there was a significant increase ( $p < 0.05$ ) in the RBC index with treatment using both the plant extracts and the standard drug. The observed increase in the RBC index in the diabetic rats following treatment with aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits suggested enhanced erythropoiesis. Some of the chemical constituents of the leaves may be responsible for the observation. For example, flavonoids stimulate the production of erythropoietin, the key hormonal

stimulant of erythropoiesis, and prevent free radicals-induced haemolysis of RBCs (Kolawole *et al*, 2017).

Elevated WBC count is a classical marker of inflammation (Hsu *et al*, 2015). The progression of the diabetic state is due to hyperglycaemia-induced oxidative stress, advanced glycation end products and the activities of cytokines and angiotensin II (González *et al*, 2023). The observed significant rise ( $p < 0.05$ ) in WBC count in diabetic rats compared to normal controls is consistent with earlier reports (Adeyi *et al*, 2021). However, the reduction in WBC count upon treatment of diabetic rats with aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits may be attributable to their anti-inflammatory action (Akgeyik *et al*, 2023). The study also showed decreased lymphocytes and increased monocytes, eosinophils and basophils (MID) cells and granulocytes in the diabetic groups when compared with normal rats. The decrease in lymphocytes may be a response to the stress associated with the diabetes since they are essential for maintenance of the body's defence immunity (Chaplin, 2010). The increase in MID cells and granulocytes may be due to involvement of these cells in the phagocytic processes against different antigens especially.

Platelets play a major role in haemostasis, wound healing, angiogenesis as well as pathogenesis of many inflammatory diseases, and its indices are indicators of microvascular complications (Chaudhary *et al*, 2022). This study showed increased platelet indices for diabetic controls compared to normal rats. The significant increase ( $p < 0.05$ ) in count was in accord with earlier findings (Essiet *et al*, 2020; Adeyi *et al*, 2021), and may have resulted from activation of the megakaryocyte-platelet system resulting in increased turnover of platelets (Akinsegun *et al*, 2014). The observed increase in plateletcrit (PCT) is naturally explainable by the raised platelet count since it represents the percentage of blood volume occupied by platelets (Essiet *et al*, 2020). It has been shown that increased Mean Platelet Volume (MPV) depicts larger platelet diameters, which can be used as a marker of platelet production and activation rates (Chandrasekhar *et al*, 2013). It can thus be opined that the significant rise of MPV in diabetic control rats compared with the normal control group resulted from increased platelet turnover and activation. The rise in the platelet distribution width (PDW) is still linkable to the activated megakaryocyte-platelet system because of platelet anisocytosis resulting from the process (Kodiatte *et al*, 2012). Consequently, treatment of diabetic rats with different preparations of the aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits yielded reduced platelet indices compared to diabetic control; implying that the effects of streptozotocin activation of the megakaryocyte-platelet pathway were attenuated.

## **CONCLUSION**

The study evaluated the phytochemical contents of aqueous extracts of *Moringa oleifera* leaves and *Tamarindus indica* fruits using HPLC. Results showed *Moringa oleifera* had the higher concentration of tannic and salicylic acids, while *Tamarindus indica* had the higher concentration of coumaric acid. The hypoglycaemic properties of the extracts were high and may have potential therapeutic applications in treating diabetes, reducing the risk of metabolic syndrome and related complications.

## **CONFLICTS OF INTEREST**

The authors declares no conflicts of Interest

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