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# Haematology and histology studies on *Moringa oleifera* leaves and bark extracts in streptozotocin-induced diabetic albino rats

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## Abstract

Alterations in haematological parameters are frequently observed in individuals with diabetes mellitus (DM). Oxidative stress has been identified as a contributing factor in the pathogenesis of organ damage and haematological dysfunction associated with DM. As a result, the potential positive impact of *Moringa oleifera*, a medicinal plant known for its antioxidant properties, on haematological parameters and kidney function in diabetic rats was investigated. A total of thirty-five rats were divided into seven groups, each consisting of five rats. Group I was administered only distilled water, while groups II to VII were induced with a single dose of 60mg/kg streptozotocin intraperitoneally. Subsequently, groups II to VI were treated with 150 mg/kg *Moringa oleifera* leaf methanol extract, 150 mg/kg *Moringa oleifera* bark methanol extract, 300 mg/kg *Moringa oleifera* leaf, 300 mg/kg *Moringa oleifera* bark, and metformin, respectively. The results showed positive modulation to most of the haematology parameters evaluated except neutrophils and lymphocytes by the treatments. The leaf extract showed a more significant modulation of platelets than other treatments. The histology of the kidney showed normal structure for all the treatments. *Moringa oleifera* especially the leaf extract is promising in the treatment of DM

**Keywords:** *Moringa oleifera;* Haematology; Kidney; Oxidative stress

## 1. Introduction

Diabetes mellitus is a chronic metabolic disorder prevalent in many countries (IHME; 2022) and is characterized by high blood sugar levels (hyperglycemia) due to impaired insulin production (Type 1) or insulin resistance (Type 2). Oxidative stress plays a critical role in the pathogenesis and complications of diabetes. It occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defences. In diabetes; high glucose levels trigger excessive ROS production; leading to damage in cells; tissues; and organs. This oxidative stress contributes to the progression of diabetes complications; such as cardiovascular disease; nephropathy; neuropathy; and retinopathy. (Zheng and Guo; 2023)

Recent studies have highlighted that managing oxidative stress through antioxidants and better glycemic control can potentially reduce diabetic complications. (Sharma; 2022). The therapeutic management of DM with minimal side effects remains a clinical challenge. However; there is growing interest in the potential use of medicinal plants as an alternative treatment for diabetes as these are commonly cheaper; less toxic and with fewer side effects. (Nissen and Wolski; 2007). The use of medicinal plants is also recommended by WHO (Roglic; 2016).

*Moringa oleifera* Lam (Moringaceae; *M. oleifera*) is a highly nutrient-rich plant with exceptional medicinal properties widely used to treat various health care problems (Farooq *et al*.; 2012). It contains three structural classes of

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phytochemicals which have several medicinal benefits. They are glucosinolates such as glucomoringin; flavonoids such as quercetin and kaempferol and phenolic acids such as chlorogenic acid (Mbikay; 2012). These phytochemicals have been reported to possess antioxidant; hypoglycemic; hypotensive; antidyslipidemic; anticancer; and anti-inflammatory properties (Amaglo *et al*.; 2010). The antioxidant properties of *Moringa oleifera* is a characteristic that is employed against the oxidative stress in DM. Also; the plants' antioxidant property plays a crucial role in maintaining overall blood health. Vitamins C and E; abundant in Moringa leaves; help protect red blood cells from oxidative stress; which can lead to hemolysis and decreased oxygen-carrying capacity. These antioxidants also support the health of immune cells; further strengthening the body's defense mechanisms. (Dhivya *et al.;* 2022).

Since haematological parameters are significantly altered in the diabetics (Bambo *et al.;* 2024); and the kidney is the organ responsible for the regulation of hematopoiesis (Leung; 2013); this research therefore aims to investigate the improvement of hematological parameters in a diabetic and the histology of the kidney using *Moringa oleifera.*

## 2. Material and methods

100% methanol solution; blended *Moringa oleifera* leaf and seed; distilled water; Streptozotocin (STZ); latex powdered examination gloves; nose masks; needles and syringes; glucometer and glucometer test strips; EDTA bottles; plain bottles; cotton wool and; standard drug (metformin).

### 2.1. Reagents and Chemicals

All chemicals and all other reagents were of analytical grade.

### 2.2. Collection and preparation of the sample

#### *2.2.1. Collection of the sample*

Fresh barks and seeds of fully grown *Moringa oleifera* were locally collected within the Federal Polytechnic Ado-Ekiti; Ekiti state. The harvested leaves of the plant were identified and authenticated at the herbarium of the Ekiti State University in Ado Ekiti and given voucher number UHAE: 2023074.

#### *2.2.2. Preparation of Moringa oleifera (MO) methanolic leaf extract*

Fresh *Moringa oleifera* leaves were air dried at room temperature for 25 days. The dried leaves were then blended to powder. 500g of the blended *Moringa oleifera* leaf sample was soaked into 2000ml of methanol for 72 hours and filtered. The filtrate was then allowed to dry under room temperature and weighed. The extract was kept in a closed container and kept inside the refrigerator for further studies.

#### *2.2.3. Preparation of Moringa oleifera (MO) methanolic bark extract*

Fresh *Moringa oleifera* barks were dried in the oven at low temperature. The dried barks were then blended to powder. 500g of the blended *Moringa oleifera* bark sample was soaked into 2000ml of methanol for 72 hours and filtered. The filtrate was then allowed to dry under room temperature and was scrapped from the plate and weighed. The extract was kept in a closed container and kept inside the refrigerator for further studies.

#### *2.2.4. Animal protocol*

Thirty five (35) Wistar rats weighing 120 g – 150 g were obtained from Ibadan; Oyo State; Nigeria. They were acclimatized in the animal house of the Department of Science Technology; The Federal Polytechnic; Ado Ekiti for 2 weeks; housed in clean wire meshed cages under standard conditions of temperature (24 ± 1$^{o}$C); relative humidity; and 12 / 12-hour light and dark cycle. They were allowed to have free access to food (commercial pelletized diet from Vital Feed Mill) and drinking water *ad libitum* daily. The rat beddings were changed and replaced every day throughout the experimental period.

### 2.3. Experimental Design

#### *2.3.1. Animal treatment*

Ethical approval (FPA/EC/23/0089) was obtained from The Federal Polytechnic Ado-Ekiti directorate of the research and the experiments were carried out with appropriate international guidelines and regulations. Thirty five male rats were divided into seven main groups. Group I was considered as negative control and received distilled water throughout the duration of the experiment. Group II was considered as positive control and received 60mg/kg STZ only

for single administration. The remaining five groups; III; IV; V VI and VII received single dose of 60mg/kg STZ and after high blood glucose was established received in addition 150mg/kg b.w of methanolic leaf extract of *Moringa oleifera*; 150mg/kg b.w of methanolic bark extract of *Moringa oleifera*; 300mg/kg mg/kg b.w of ordinary leaf of *Moringa oleifera* (unextracted); 300mg/kg b.w of ordinary bark (unextracted) and 21.4 mg/kg b.w of metformin respectively for two weeks.

*2.3.2. Dissection of Rats*

Twenty-four hours after the last administration; the rats were dissected and portion of blood was collected into EDTA bottles for haematological analysis.

The kidneys were excised using scissors and forceps and trimmed of fatty tissues for histopathological examination.

*2.3.3. Haematological analysis*

Haematological analysis on red blood cell (RBC); white blood cell (WBC); Packed cell volume (PCV); and Platelets were carried out according to the method of Dacie and Lewis (2001).

*2.3.4. Histopathology Examination on kidney*

A histopathology examination of the kidney was performed using a modified Avwioro (2010) method. Tissue processor (leica tp1020) was used for the processing. Stations one and two contained formol saline while three to seven contained 70 %; 80 %; 90 %; 95 % of ethanol and absolute ethanol respectively. The tissues were also dehydrated by passing through stations eight and nine which contained xylene. Infiltration and impregnation was done by transferring to 3 wax baths. These were stained with haematoxylin and eosin technique. Leica SCN software was used for the evaluation.

## 3. Results

Table 1 shows the results of the haematological parameters after 14 days of treatment with *Moringa oleifera*. The packed cell volume (PCV) of the induced but not treated diabetic rat was very low compared with the non-induced control. However; all the treatments except treatment with the leaf extract increased the PCV to a level greater than the control. The treatments is shown to increase the haemoglobin levels (HB) that was lowered in the induced but not treated animals. All other parameters lowered in the induced animals (MCV; RBC; WBC) were increased to a comparable level with the control in the treated animals. The platelets and the mean corpuscular haemoglobin concentration (MCHV) that was increased in the induced but not treated animals became lowered in all the treated animals. The monocytes; basophils and eosinophils levels remained the same in all the groups including the control;

The histopathology results of the kidney are shown in Figure 1. It showed that all the kidneys of the groups were normal except the induced but not treated group

**Table 1** Haematological Analysis of the diabetic rats after 14 days treatment with *Moringa oleifera*

| **Parameters/ Groups** | **G 1** | **G 2** | **G 3** | **G 4** | **G 5** | **G 6** | **G 7** |
|---|---|---|---|---|---|---|---|
| PCV(%) | 43.00± 1.081 | 32.70± 2.024 | 29.50±1.105 | 47.50±1.063 | 44.00± 2.058 | 48.50± 1.303 | 52.00± 1.039 |
| HB(g/dL) | 20.05± 1.058 | 12.50± 1.080 | 17.35± 1.063 | 15.95± 0.413 | 16.50± 0.363 | 16.25± 1.063 | 19.85± 1.063 |
| MCV (fL) | 71.00± 2.042 | 39.50± 1.213 | 55.50± 1.070 | 52.10± 1.014 | 52.05± 2.004 | 50.05± 1.217 | 52.00± 1.102 |
| MCHC (g/dL) | 20.90± 2.013 | 36.20± 2.001 | 18.55± 2.170 | 22.95± 0.511 | 27.30± 1.203 | 22.75± 1.031 | 23.25± 0.506 |
| RBC($X10^6/mm^3$ | 14.55± 0.117 | 7.83± 0.273 | 15.30± 0.155 | 19.10± 0.307 | 18.50± 0.202 | 14.80± 0.160 | 16.25± 0.300 |
| WBC($X10^3/mm^3$) | 13.12± 0.310 | 8.45± 0.109 | 11.95± 0.127 | 15.20± 0.211 | 14.91± 0.203 | 19.20± 0.354 | 14.90± 0.114 |
| Neutrophil % | 24.00± 1.103 | 38.50± 0.206 | 36.00± 1.071 | 42.00± 2.011 | 40.50± 1.302 | 32.50± 1.210 | 32.50± 2.144 |
| Lymphocyte% | 74.50± 2.190 | 63.00± 1.162 | 62.50± 2.203 | 57.00± 1.604 | 58.50± 1.105 | 66.50± 2.115 | 66.00± 3.011 |
| Monocyte % | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Eosinophil % | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Basophil % | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| Platelet($X10^3$ /ml | 170± 3.121 | 387.50± 2.305 | 146.50± 2.140 | 340.50± 5.004 | 247.00± 3.204 | 382.50± 2.530 | 352.00± 2.713 |

Values are expressed as mean ± standard deviation. G1 – Non Diabetic Control; G2 – Diabetic Control; G3 - 150mg/kg b.w of methanolic leaf extract of *Moringa oleifera*; G4-150mg/kg b.w of methanolic bark extract of *Moringa oleifera*; G5-300mg/kg mg/kg b.w of ordinary leaf of *Moringa oleifera* (unextracted); G6-300mg/kg b.w of ordinary bark (unextracted) G7-21.4 mg/kg b.w of metformin. PCV- packed cell volume; HB – haemoglobin; MCHC- mean corpuscular hemoglobin concentration; RBC – red blood cell; WBC – white blood cell

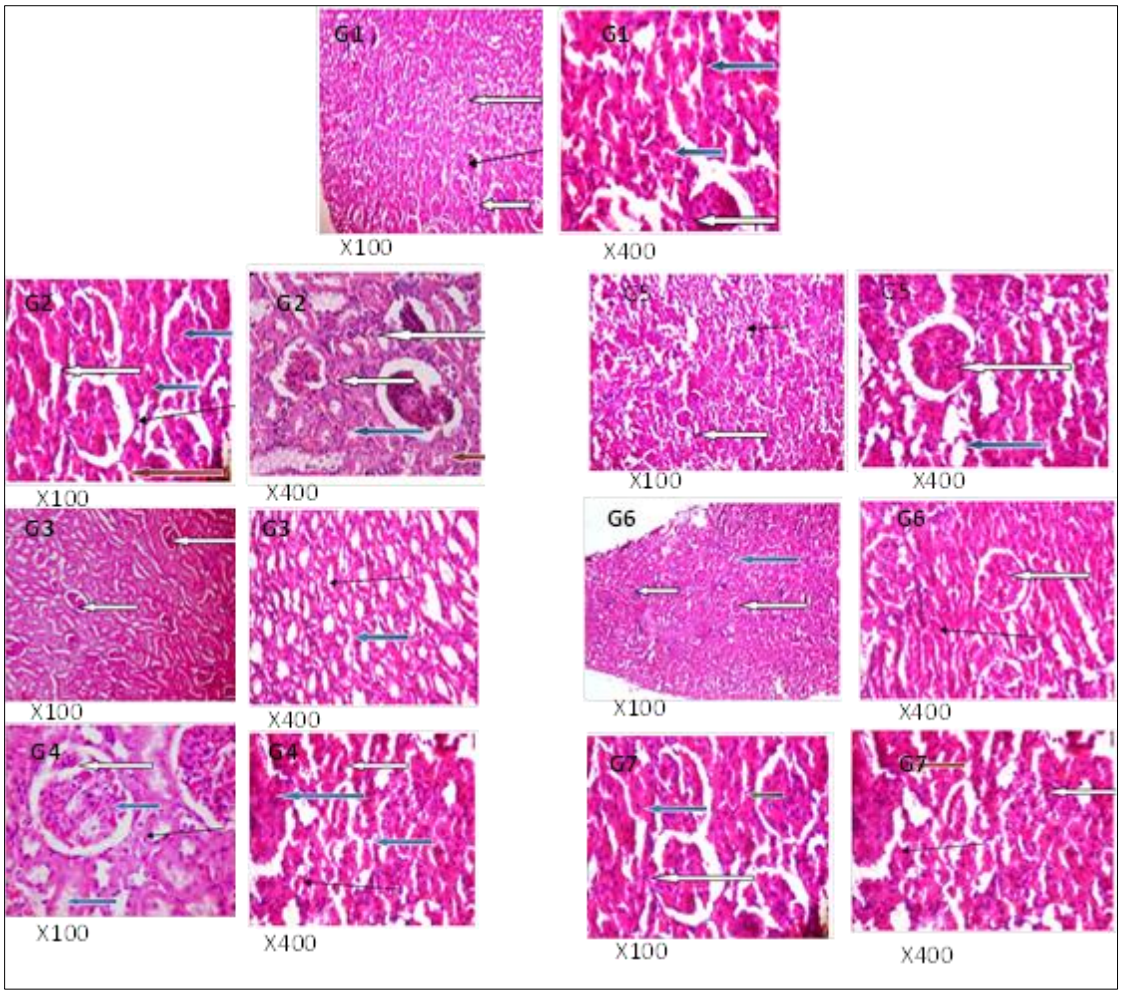


**Figure 1** Photomicrograph of rat kidney sections stained with hematoxylin and eosin and viewed at X100 and X400 magnifications.

- G1 - Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).
- **G2 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing moderate architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); some renal tubules appear mildly degenerated (red arrow); while other tubules appear normal (blue arrow); the interstitial spaces show mild vascular congestion (slender arrow).
- **G3 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).
- **G4 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).
- **G5 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).
- **G6 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and

capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).

- **G7 -** Photomicrographs of kidney sections stained by Haematoxylin and Eosin showing normal architecture as seen in lower magnification x100; the renal cortex show normal glomeruli with normal mesengial cells and capsular spaces (white arrow); the renal tubules appear normal (blue arrow); the interstitial spaces appear normal (slender arrow).

## 4. Discussion

Hematological modifications are intricately associated with the generation of reactive oxygen species (ROS) consequent to prolonged hyperglycemia in individuals with diabetes. The excessive production of ROS precipitates oxidative stress; culminating in tissue impairment; haematological modifications; and dysfunction of endothelial and erythrocyte cells. (Arkew *et al.;*2021; Mahdi *et al.;* 2021). Streptozotocin induction caused a notable reduction in red blood cells; packed cell volume (PCV or haematocrit); total white blood cell and platelet counts when compared to the control group (Table 1).

As observed; the extracts had some positive effects on the haemopoietic system of the test rats. This was manifested by modulation of red blood cells; packed cell volume (PCV or haematocrit); total white blood cell and platelet counts following administration of the plant extracts to the rats. The percentage of PCV increased for the animals treated with plant extract when compared with the untreated group. Examination of haematological parameters; including red cells (erythrocytes); white cells (leucocytes); and platelets (thrombocytes); along with factors related to them; provides valuable information on inflammation; necrosis; various infections of visceral organs; and the presence of stress factors (Betancourt-Alonso *et al.;* 2011). Additionally; it plays a significant role in assessing the physiological; nutritional; and pathological status of an organism. (Odeghe *et al*.; 2012). The results suggest its potential role in managing haematology parameters in diabetes. The raised haematocrit is an indication of haemoconcentration which may be due to increased RBC mass. The value obtained for RBC count in the treatment groups also increased notably when compared to the untreated group.

An increase in WBC count was also recorded for the treatment groups when compared to the control as against WBC of the streptozotocin-induced group where a reduction in WBC was recorded. Also; the value of lymphocytes for the group II animals (induced group) which were given streptozotocin alone reduced when compared with the control group. However; the groups treated with the standard drug and unextracted bark of the *Moringa oleifera* had their platelet levels increased while all the treated groups had elevated levels of RBC. According to a study by Abdel-Latif *et al*. (2021); administering *Moringa oleifera* extracts in laboratory animals significantly increased total WBC count; particularly lymphocytes; suggesting enhanced immune system activity. This effect is attributed to the plant's ability to reduce inflammation and oxidative stress; key contributors to immune dysfunction. Also; a study by Dhivya *et al.* (2022) demonstrated that rats supplemented with Moringa extract showed reduced oxidative stress markers and improved RBC membrane integrity; indicating the protective effect of the plant on blood cells.

A notable decrease in HB concentrations was observed in group 2 (Diabetic control) relative to group 1 (non-diabetic control) whereas a notable increase in haemoglobin concentrations was observed in groups treated with all extracts of *Moringa oleifera* relative to groups 2 (Diabetic control). One of the key components of *Moringa oleifera* is its high iron content; which makes it particularly valuable for addressing iron deficiency. Studies suggest that the leaves of *Moringa oleifera* are rich in iron (approximately 28.2 mg/100 g); which is crucial for the synthesis of haemoglobin; a protein in red blood cells responsible for oxygen transport. Supplementation with *Moringa oleifera* has shown promise in improving haemoglobin levels; particularly in anaemic patients or populations with nutritional deficiencies. A study conducted by Kasolo *et al.* (2010) demonstrated that oral administration of moringa leaf powder significantly increased haemoglobin concentrations and RBC counts in experimental animals; suggesting its potential role in promoting erythropoiesis; the production of red blood cells.

Streptozotocin induction significantly increased neutrophil and decreased lymphocyte count when the diabetic control is compared with the treated animals. Treatment with different extracts of *Moringa oleifera* did not bring the neutrophil to a normal count when compared with the non-diabetic control. The same trend is observed in the lymphocyte but treatment with the standard drug and unextracted bark elevated the value a little above the diabetic control. Also; the platelets levels were significantly increased to about a double fold in many of the treatments. However; the group treated with the leaf extract had a notably lower value compared to the non-diabetic control. Platelet hyperactivity and increased reactivity are observed in diabetic individuals; elevating the propensity for thrombotic incidents; notably cardiovascular complications such as stroke and myocardial infarction. Elevated blood glucose levels induce oxidative stress; thereby augmenting platelet aggregation and compromising endothelial function; further fostering coagulation.

Concurrently; insulin resistance and chronic inflammation exacerbate this platelet dysfunction; underscoring the necessity of antiplatelet therapies in mitigating cardiovascular risks in diabetes. (Kaur *et al.;* 2018; Shrimali *et al.;* 2022 and Vnik *et al.;* 2001). These effects are primarily attributed to the plant's rich nutritional and phytochemical composition documented in the literature; which includes iron; flavonoids; vitamins; and antioxidants.

Diabetic nephropathy (DN); also called diabetic kidney disease (DKD); is a common complication of diabetes mellitus (DM). It is the primary cause of chronic kidney disease (CKD) and can lead to end-stage renal disease (ESRD); which is associated with increased morbidity and mortality in diabetic patients. Managing and monitoring kidney health is crucial for individuals with diabetes to prevent the progression of diabetic nephropathy and its associated complications (Samsu; 2021).

Natural products; primarily from herbal sources; have long been explored as sources of drugs to treat a variety of major diseases. To date; significant efforts have been made to support and validate the potential effectiveness of natural and synthetic products in experimental studies and clinical applications; and indicate the antioxidant effects on the kidney (Talas *et al*.; 2009; Talas *et al.;* 2014). In preclinical studies; many natural products have recently been reported to alleviate kidney disease by modulating oxidative stress and inflammation (Hu *et al.;* 2023).

Histopathological changes of the kidney showed that renal tubules appear mildly degenerated and the interstitial spaces showed mild vascular congestion are indicative of nephrotoxicity (Sahreen *et al*.; 2010; Nabeshima *et al*.; 2006). Severe histoarchitectural distortion of the kidney tissue observed as mildly degenerated renal tubules and mild vascular congestion in the kidney section of Wistar rats treated with streptozotocin only when compared with the kidney sections of the control is indicative of streptozotocin-related nephrotoxicity. Kidneys of rats treated with *Moringa oleifera* extracts and control rats showed normal architecture; normal glomeruli with normal mesengial cells and capsular spaces; the renal tubules appear normal and the interstitial spaces appear normal. This suggests the protective nature of *Moringa oleifera* on the kidneys of the diabetic rats.

## 5. Conclusion

This study showed that *Moringa oleifera* has modulatory potential on the haematological parameters in streptozotocin-induced; diabetic rats lending credence to the use of these plant extracts in folk medicine for the management of diabetes. The methanol leaf extract was able to normalize the high platelet level induced by diabetes while it remained high in other treatments including metformin. The histology results of the kidney suggest that all the treatments prevent streptozotocin-induced diabetic nephropathy in Wistar rats. The nephroprotective activity of the plant extracts; which could be of therapeutic potential; may be consequent to the antioxidant activities of constituent phytochemicals. Therefore; It is recommended that *Moringa oleifera* act as an adjunct in chronic treatment of diabetes mellitus.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors declare that there is no conflict of interest.

### *Statement of ethical approval*

The animal use and Care Committee of the Federal Polytechnic Ado Ekiti after critical evaluation and review approved this study (approval number FPA/EC/23/0089) National Institutes of Health's Guidelines for using and caring for laboratory animals and relevant methods were followed to ensure that the animals were not subjected to excessive stress and discomfort during this experiment.

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