In Vivo Hypoglycemic Activity of Aqueous Leaf and Root Extracts of *Macaranga Barteri* Müll. Arg. (Euphorbiaceae) In Swiss Albino Mice

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Abstract

Background: Macaranga barteri Müll. Arg. is a perennial plant in the family Euphorbiaceae and is used in African traditional medicine for the management of several ailments, including diabetes. Although the leaves and stem bark have been studied for various pharmacological activities, little is known about the therapeutic value of the roots. Objective: This study evaluated the in vivo hypoglycemic activity of aqueous leaf and root extracts of M. barteri in alloxan-induced diabetic Swiss albino mice and assessed their safety following repeated oral administration. Materials and **Methods**: Fresh leaves and roots of M. barteri were collected, authenticated, air-dried, and extracted with distilled water by hot maceration. Diabetes was induced in Swiss albino mice using

intraperitoneal alloxan monohydrate, and diabetic animals were treated orally with leaf or root extracts at doses of 50, 100, and 200 mg/kg body weight for seven days. Glibenclamide served as the reference drug. A 28-day repeated-dose oral toxicity study was also conducted in healthy mice using doses of 200, 346, and 600 mg/kg body weight. Body weight, relative organ weights, hematological indices, and biochemical markers of liver and kidney function were evaluated. **Results:** Phytochemical screening revealed the presence of alkaloids, tannins, flavonoids, terpenoids, steroids, saponins, and coumarins. Both leaf and root extracts significantly reduced blood glucose levels in alloxan-induced diabetic mice, with effects comparable to glibenclamide. The leaf extract showed the greatest glucose-lowering effect at 200 mg/kg body weight, whereas the root extract was most active at 100 mg/kg body weight. In the 28-day toxicity study, neither extract produced marked adverse effects on body weight, organ-to-body weight ratios, hematological parameters, or biochemical markers of hepatic and renal function.

Conclusion: The findings demonstrate that aqueous leaf and root extracts of M. barteri possess significant hypoglycemic activity in diabetic mice and appear relatively safe following repeated oral administration at the tested doses. These results support the traditional use of M. barteri in the management of hyperglycemia and provide a basis for further pharmacological and clinical investigations.

Keywords: Macaranga barteri, hypoglycemic activity, diabetes mellitus, medicinal plants, toxicity, Swiss albino mice

1. Introduction

Diabetes mellitus (DM) is one of the most significant global public health challenges of the twenty-first century. In 2021, an estimated 537 million adults aged 20–79 years were living with diabetes worldwide, compared with approximately 108 million in 1980. This number is projected to increase to 643 million by 2030 and 783 million by 2045 [1][2]. Despite extensive research and numerous interventions aimed at preventing and controlling diabetes, the global burden of the disease continues to rise, with the majority of reported cases occurring in low- and middle-income countries (LMICs) [3].

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, defective insulin action, or both [4]. Insulin, a hormone produced by the pancreatic β-cells, plays a critical role in regulating glucose uptake and utilization

by body tissues for energy production or storage. Defects in insulin secretion or action disrupt carbohydrate, lipid, and protein metabolism, resulting in elevated blood glucose levels and long-term metabolic complications [5].

Type 1 diabetes mellitus (T1DM) results from immune-mediated destruction of pancreatic β-cells, leading to an absolute deficiency of insulin secretion [4]. In contrast, Type 2 diabetes mellitus (T2DM) develops primarily because of insulin resistance combined with progressive β-cell dysfunction, resulting in chronic hyperglycemia [2][4]. T2DM accounts for more than 90% of all diabetes cases globally [2].

According to current diagnostic criteria, diabetes can be confirmed by any of the following: glycated hemoglobin (HbA1c) ≥6.5%; fasting plasma glucose ≥126 mg/dL (7.0 mmol/L) after at least 8 hours of fasting; a 2-hour plasma glucose level ≥200 mg/dL (11.1 mmol/L) during a 75-g oral glucose tolerance test (OGTT); or a random plasma glucose concentration ≥200 mg/dL (11.1 mmol/L) in individuals presenting with classic symptoms of hyperglycemia, including polyuria, polydipsia, polyphagia, unexplained weight loss, or hyperglycemic crisis [2][6]. Nevertheless, nearly half of all individuals living with diabetes worldwide remain undiagnosed, thereby increasing their risk of developing severe complications before receiving appropriate treatment [2][7].

The increasing prevalence of diabetes has been attributed to rapid urbanization, industrialization, population aging, sedentary lifestyles, obesity, and the widespread consumption of energy-dense and unhealthy diets [8]. These factors have contributed substantially to the growing global burden of diabetes and its associated complications.

Diabetes is currently among the ten leading causes of death worldwide. Together with cardiovascular diseases, cancers, and chronic respiratory diseases, it contributes to approximately 80% of premature deaths resulting from non-communicable diseases (NCDs) [9]. Beyond its direct health consequences, diabetes substantially increases the risk of cardiovascular disease, stroke, chronic kidney disease, chronic liver disease, infections, and several forms of cancer. Consequently, diabetes has one of the greatest adverse impacts on global health-adjusted life expectancy [9]. Furthermore, the management of diabetes and its associated microvascular and macrovascular complications imposes a considerable economic burden on individuals, healthcare systems, and national economies. Although reliable epidemiological data remain limited across many African countries, the International Diabetes Federation (IDF) estimates that diabetes accounts for

approximately 7% of the continent's healthcare expenditure [10]. Diabetes-related healthcare costs in Africa were estimated at approximately USD 3.4 billion in 2015 and are projected to increase to USD 5.5 billion by 2040. These estimates may underestimate the true economic burden because nearly two-thirds (66.7%) of people living with diabetes in Africa are believed to be undiagnosed [10].

Current management of diabetes relies largely on hypoglycemic agents, which include both synthetic and naturally derived compounds. These agents act through various mechanisms, such as stimulating insulin secretion from pancreatic β-cells, reducing hepatic glucose production, enhancing peripheral glucose uptake, increasing insulin sensitivity, and delaying intestinal glucose absorption. Common synthetic antidiabetic medications include insulin preparations, sulfonylureas, biguanides, thiazolidinediones, α-glucosidase inhibitors, and sodium-glucose cotransporter-2 (SGLT2) inhibitors. However, the long-term use of these medications may be associated with adverse effects such as hypoglycemia, lactic acidosis, myalgia, blurred vision, dyspepsia, and other undesirable reactions, thereby limiting their clinical use in some patients [6][11]. Consequently, there is increasing interest in identifying safer, more affordable, and effective alternative therapies for diabetes management.

Medicinal plants have received considerable attention as potential sources of novel antidiabetic agents. Numerous experimental and clinical studies have demonstrated the therapeutic potential of plant-derived phytochemicals in the prevention and management of diabetes mellitus [12][13][14]. Herbal medicines remain widely used in many developing countries because of their accessibility, affordability, cultural acceptance, and perceived safety and efficacy [15].

Macaranga barteri Müll.-Arg. is a perennial angiosperm tree or shrub belonging to the family Euphorbiaceae and is widely distributed throughout tropical and subtropical regions of Africa [12][16][17]. The plant is commonly known as "Aarasa" and "Owariwa" among the Yoruba people of Nigeria, "Opam-kokoo" among the Akan people of Ghana, and "Guu" among the Mano tribe in Liberia [12][18]. Ethnomedicinal reports indicate that preparations made from the leaves and stem bark, either as powders or decoctions, have traditionally been used as vermifuges and febrifuges in Nigerian and Congolese folk medicine. In Sierra Leone and Liberia, leaf decoctions are used as laxatives, haematinics, and for the treatment of sexually transmitted infections [12][18][19]. In addition, *M. barteri*, either alone or in combination with other *Macaranga* species, has traditionally been used for the management of persistent cough, bronchitis, stomatitis, gastric ulcers, diarrhea,

edema, and arthritis in several African communities [12][20]. Scientific investigations have further demonstrated that extracts from the leaves and stem bark possess antimicrobial, anti-inflammatory, antihyperalgesic, antioxidant, cytotoxic, and antiproliferative activities [12][17][21].

Several bioactive phytochemicals with diverse pharmacological properties have been isolated from the leaves and stem bark of *M. barteri*. However, the therapeutic potential of the roots remains largely unexplored, and limited scientific evidence exists regarding the hypoglycemic effects of orally administered aqueous extracts of the plant. Therefore, the present study investigated the hypoglycemic activity of aqueous leaf and root extracts of *M. barteri* in Swiss albino mice and compared the antidiabetic efficacy of the two plant extracts.

2. Materials and Methods

2.1 Materials

All chemicals and reagents used were of analytical grade and obtained from Legacy Lab Africa Ltd., Nairobi, Kenya. Laboratory equipment included a rotor mill (SR 300), freeze dryer (UMS-12PT), refrigerated centrifuge (UMS-GL16), Reflotron Plus biochemistry analyzer, and Mindray BC-5000 clinical chemistry analyzer.

2.2 Plant Collection and Authentication

Fresh leaves and roots of *Macaranga barteri* Müll.-Arg. were collected from Ipara Remo Township, Ogun State, Nigeria, based on ethnobotanical information from previous studies [12][18][21]. The plant was authenticated at the Department of Botany, University of Ibadan, Nigeria, and a voucher specimen (UHI-23098) was deposited in the University Herbarium. Plant materials were air-dried at room temperature for 24 days, pulverized into fine powder, and stored in airtight containers until extraction.

2.3 Preparation of Aqueous Extracts

Aqueous extracts were prepared by hot maceration to simulate the traditional method of preparation. Briefly, 250 g each of powdered leaves and roots were extracted separately with distilled water at optimized temperatures of 40°C (leaves) and 65°C (roots) for 45 minutes. Extraction was performed in triplicate to maximize yield. The filtrates were centrifuged, freeze-

dried, and stored at −10°C until use. Percentage yield was calculated as the ratio of crude extract weight to the initial plant material weight.

2.4 Experimental Animals

Healthy six-week-old Swiss albino mice (both sexes; mean body weight 25 g) were obtained from the Animal House, Department of Biochemistry, Microbiology and Biotechnology, Kenyatta University, Kenya. Animals were housed under standard laboratory conditions (25 ± 2°C, 45–55% humidity, and a 12-h light/dark cycle) with free access to standard rodent pellets and water. The mice were acclimatized for 72 hours before experimentation. Animal handling complied with internationally accepted guidelines for the care and use of laboratory animals [22][23].

2.5 Experimental Design and Induction of Diabetes

A randomized controlled design was adopted. Forty-five mice were randomly allocated into nine groups (n = 5), comprising a normal control, diabetic control, positive control (glibenclamide, 3 mg/kg body weight), and six treatment groups receiving aqueous leaf or root extracts at doses of 50, 100, and 200 mg/kg body weight. Treatments were administered orally once daily for seven days.

Experimental diabetes was induced after overnight fasting by a single intraperitoneal injection of freshly prepared alloxan monohydrate (186.9 mg/kg body weight). Seventy-two hours after induction, fasting blood glucose was measured using an On Call Plus® glucometer, and mice with blood glucose levels ≥200 mg/dL (11.1 mmol/L) were considered diabetic and included in the study. Blood glucose levels were monitored before treatment and after seven days of treatment [24].

2.6 Preparation of Extract Doses

Freeze-dried extracts were reconstituted in normal saline to obtain doses of 50, 100, and 200 mg/kg body weight, while glibenclamide (3 mg/kg body weight) served as the reference drug. Dose selection followed the logarithmic dose progression method, and all treatment solutions were freshly prepared and stored at −20°C before administration.

2.7 Toxicity Evaluation

A 28-day repeated-dose oral toxicity study was conducted according to OECD Guideline 407 [25][26]. Healthy Swiss albino mice were randomly assigned into seven groups (n = 5) and administered aqueous leaf or root extracts at doses of 200, 346, or 600 mg/kg body weight, while

the control group received normal saline. Animals were observed daily for clinical signs of toxicity, behavioural changes, mortality, and changes in body weight.

At the end of the study, mice were euthanized, and the liver, kidneys, pancreas, heart, lungs, and spleen were excised, weighed, and their relative organ weights calculated.

2.8 Hematological and Biochemical Analyses

Blood samples were collected by cardiac puncture following euthanasia. Hematological parameters, including red blood cell count, white blood cell count, haemoglobin concentration, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, and differential leukocyte counts, were determined using an automated hematology analyzer according to standard procedures [27][28].

Serum biochemical analyses, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and urea, were performed using an automated clinical chemistry analyzer following standard laboratory procedures [28].

2.9 Qualitative Phytochemical Screening

Qualitative phytochemical screening of the aqueous leaf and root extracts was performed using standard methods to detect alkaloids [29][30], tannins and phenols [31][32], flavonoids [33], terpenoids [33][29], steroids [31][32], saponins [33][29], and coumarins [34]. Results were recorded as absent (−), present (+), or strongly present (++).

2.10 Ethical Approval

Ethical approval for plant collection was obtained from the Plant Ethics Committee of the University of Ibadan, Nigeria (APR Ref: 2022/2023). Animal experiments were approved by the Kenyatta University Animal Care and Use Committee (KUACUC Ref: PKUA/008/008).

2.11 Statistical Analysis

Data were entered into Microsoft Excel 2019 and analyzed using IBM SPSS Statistics version 20. Results are presented as mean ± standard error of the mean (SEM). One-way analysis of variance (ANOVA) followed by Tukey's post hoc test was used to compare group means, while the unpaired

Student's *t*-test was used to compare the hypoglycemic effects of leaf and root extracts at corresponding doses. Statistical significance was considered at $p \leq 0.05$.

Recommendation for Journal Publication

Since you are preparing this manuscript for publication, I also recommend **converting all author–date citations to sequential Vancouver citations** (e.g., **(Asante-Kwatia et al., 2019; Hwang, 2017; Segun et al., 2019) → [22–24]**) to ensure consistency with the Vancouver style you are using throughout the article. This will give the manuscript a professional, publisher-ready appearance.

3. Results

Table 1: Grouping of Mice for Toxicity Study

Treatment group	Oral treatment received	Mean body weight (grams)
Group I, control	0.1 mL of normal saline daily	24.24
Aqueous leaves extracts administration		
Group II	1.2g (200 mg/kg b. wt.)	23.85
Group III	2g (346 mg/kg b.wt.)	23.08
Group IV	3.4g (600 mg/kg b.wt.)	22.52
Aqueous roots extracts administration		
Group V	1.1g (200 mg/kg b.wt.)	22.04
Group VI	1.95g (346 mg/kg b.wt.)	22.56
Group VII	3.7g (600 mg/kg b.wt.)	24.63

Table 1 presents the grouping of mice used for the toxicity study, showing the treatment given to each group and their mean body weight. The control group, which received 0.1 mL of normal saline daily, had a mean body weight of 24.24 g. For the groups treated with the aqueous leaves extract, the mean body weight showed a slight gradual decrease as the dose increased, moving from 23.85 g in Group II at 200 mg/kg body weight, to 23.08 g in Group III at 346 mg/kg body weight, and then to 22.52 g in Group IV at 600 mg/kg body weight. This suggests that increasing doses of the leaves extract may have been associated with a small reduction in body weight.

In the groups treated with the aqueous roots extract, a different pattern was observed. Group V, which received 200 mg/kg body weight, had a mean body weight of 22.04 g, while Group VI at 346

mg/kg body weight had a slightly higher mean body weight of 22.56 g. Interestingly, Group VII, which received the highest root extract dose of 600 mg/kg body weight, recorded the highest mean body weight of 24.63 g among all the groups, even slightly higher than the control.

On the overall, the table shows that body weight changes were not completely uniform across all treatment groups. While the leaves extract appeared to show a dose-related reduction in body weight, the roots extract did not follow the same pattern, with the highest root dose showing an increase in mean body weight

Table 2: Lyophilized yields of aqueous extractions of *M. barteri* leaves and roots

S/N	Extract	Yield (g)	Color	% Yield
1.	Leaves	17.35	Dark brown	6.94
2.	Roots	15.425	Brownish-yellow	6.17

Table 2 shows the lyophilized yields obtained from the aqueous extraction of *M. barteri* leaves and roots. The leaves produced a slightly higher extract yield of 17.35 g with a dark brown color, corresponding to a percentage yield of 6.94%. In comparison, the roots produced 15.425 g of extract, which was brownish-yellow in color, with a slightly lower percentage yield of 6.17%. Overall, the findings suggest that the leaves gave a better extraction yield than the roots under the same aqueous extraction process, although the difference was not very large. This may indicate that the leaves contain a slightly higher amount of water-soluble constituents than the roots.

Table 3: Shows the Qualitative Preliminary Phytochemical Screening of the presence of some major secondary metabolites of M. barteri Leaf and Root Extracts.

Phytochemical	Plant part	
	Leaves	Roots
Alkaloids	+	-
Flavonoids	++	++
Tannins	++	++
Saponins/phenols	++	++
Coumarins	-	+
Steroids	++	++
Terpenoids	++	++

++ (Present), + (sparingly present), - (Absent)

Presents in Table 3 is the qualitative preliminary phytochemical screening of *M. barteri* leaf and root extracts, showing the presence or absence of major secondary metabolites in both plant parts. The results indicate that flavonoids, tannins, saponins/phenols, steroids, and terpenoids were present in both the leaves and roots, suggesting that these two parts of the plant share several important bioactive compounds. Among these, flavonoids, tannins, saponins/phenols, steroids, and terpenoids were all strongly present in both extracts, as indicated by the double positive sign. Alkaloids were sparingly present in the leaves but completely absent in the roots, while coumarins were absent in the leaves but sparingly present in the roots. Overall, the findings show that both the leaf and root extracts of *M. barteri* contain a rich range of phytochemicals, although there are slight differences in the distribution of alkaloids and coumarins between the two plant parts.

Table 4: Effect of *M. barteri* Leaf Extract on Paw Edema in Experimental Animals Across Different Time Intervals

Groups	Hour 0	Hour 1	Hour 2	Hour 3	Hour 4	Hour 5	Hour 6	Hour 24	Day 7
Normal control	5.76 ± 0.45^{b}	5.96 ± 0.27^{d}	5.58 ± 0.35^{d}	5.20 ± 0.37^{e}	4.76 ± 0.47^{e}	4.26 ± 0.23^{e}	4.70 ± 0.47^{d}	6.30 ± 0.19^{d}	5.92 ± 0.33^{d}
Positive control	27.72 ± 1.61^{a}	23.22 ± 1.02^{bc}	17.84 ± 0.46^{c}	13.34 ± 0.29^{c}	11.60 ± 0.35^{d}	10.36 ± 0.31^{d}	9.26 ± 0.25^{c}	8.74 ± 0.26^{c}	9.10 ± 0.22^{c}
Negative control + A	29.98 ± 0.73^{a}	27.48 ± 0.66^{a}	30.00 ± 0.77^{a}	28.80 ± 0.59^{a}	27.90 ± 0.45^{a}	26.90 ± 0.47^{a}	26.16 ± 0.41^{a}	26.86 ± 0.41^{a}	25.78 ± 0.44^{a}
50mg/kg b.wt.. L + A	28.84 ± 1.14^{a}	24.06 ± 1.07^{abc}	20.80 ± 0.25^{b}	17.66 ± 0.39^{b}	17.10 ± 0.46^{b}	14.20 ± 0.19^{b}	13.84 ± 0.32^{b}	13.60 ± 0.25^{b}	11.60 ± 0.37^{b}
100mg/kg b.wt. L + A	27.64 ± 1.45^{a}	26.04 ± 0.51^{ab}	19.54 ± 0.22^{bc}	14.20 ± 0.47^{c}	14.04 ± 0.30^{c}	12.56 ± 0.16^{c}	12.38 ± 0.25^{b}	12.86 ± 0.10^{b}	11.02 ± 0.32^{b}

Table 4 shows the changes in paw edema across the different treatment groups from hour 0 to day 7. The normal control group maintained very low paw edema values throughout the study period, showing only slight fluctuations and confirming the absence of induced inflammation. In contrast, the positive control group started with a high paw edema value at hour 0, but the swelling gradually reduced over time, reaching much lower levels by hour 24 and day 7. This suggests that the standard treatment used in the positive control was effective in reducing inflammation.

The negative control group, which received the inflammatory agent without treatment, recorded the highest paw edema values throughout the observation period, with only a slight reduction over time. This indicates that inflammation remained severe in the absence of any active treatment. For the groups treated with *M. barteri* leaf extract, both doses showed a gradual reduction in paw edema from hour 1 onward. However, the reduction was more pronounced in the group treated with 100 mg/kg body weight compared with the 50 mg/kg group, especially from hour 2 to day 7. By the end of the study, both extract-treated groups had much lower edema values than the negative control, although they were still higher than the positive and

Table 5: Effects of Aqueous Root Extracts of M. Barteri on Blood Sugar Levels In Alloxan-Induced Diabetic Mice.

Groups	Hour 0	Hour 1	Hour 2	Hour 3	Hour 4	Hour 5	Hour 6	Hour 24	Day 7
Normal control	5.76 ± 0.45[b]	5.96 ± 0.27[d]	5.58 ± 0.35[d]	5.20 ± 0.37[e]	4.76 ± 0.47[d]	4.26 ± 0.23[d]	4.70 ± 0.47[d]	6.30 ± 0.19[e]	5.92 ± 0.33[d]
Positive control	27.72 ± 1.61[a]	23.22 ± 1.02[bc]	17.84 ± 0.46[c]	13.34 ± 0.29[d]	11.60 ± 0.35[c]	10.36 ± 0.31[c]	9.26 ± 0.25[c]	8.74 ± 0.26[d]	9.10 ± 0.22[c]
Negative control + A	29.98 ± 0.73[a]	27.48 ± 0.66[a]	30.00 ± 0.77[a]	28.80 ± 0.59[a]	27.90 ± 0.45[a]	26.90 ± 0.47[a]	26.16 ± 0.41[a]	26.86 ± 0.41[a]	25.78 ± 0.44[a]
50mg/kg b.wt. R + A	30.98 ± 0.46[a]	25.72 ± 1.14[ab]	20.32 ± 0.39[b]	17.98 ± 0.35[b]	16.50 ± 0.50[b]	12.92 ± 0.33[b]	12.76 ± 0.33[b]	12.92 ± 0.23[b]	10.46 ± 0.20[b]

Blood glucose levels (mmol/L)

Table 5 shows the effect of the aqueous root extract of *M. barteri* on blood sugar levels in alloxan-induced diabetic mice over time. The normal control group maintained low blood glucose values throughout the study, which reflects the normal blood sugar range in healthy mice. In contrast, the negative control group recorded the highest blood glucose levels from hour 0 to day 7, with only a slight reduction over time, indicating that diabetes remained uncontrolled in the absence of

treatment. The positive control group showed a clear and steady decrease in blood glucose levels from hour 0 to day 7, confirming the effectiveness of the standard antidiabetic treatment used in the study. For the group treated with 50 mg/kg body weight of the aqueous root extract, blood glucose levels were initially high at hour 0, similar to the diabetic untreated group, but they gradually decreased as time progressed. The reduction became more noticeable from hour 2 onward and continued up to day 7, where the blood sugar level dropped to 10.46 mmol/L. Although this value was still higher than that of the normal control group, it was much lower than that of the negative control group and close to the positive control result. Overall, the findings suggest that the aqueous root extract of *M. barteri* has blood sugar-lowering activity and may possess antidiabetic potential in alloxan-induced diabetic mice.

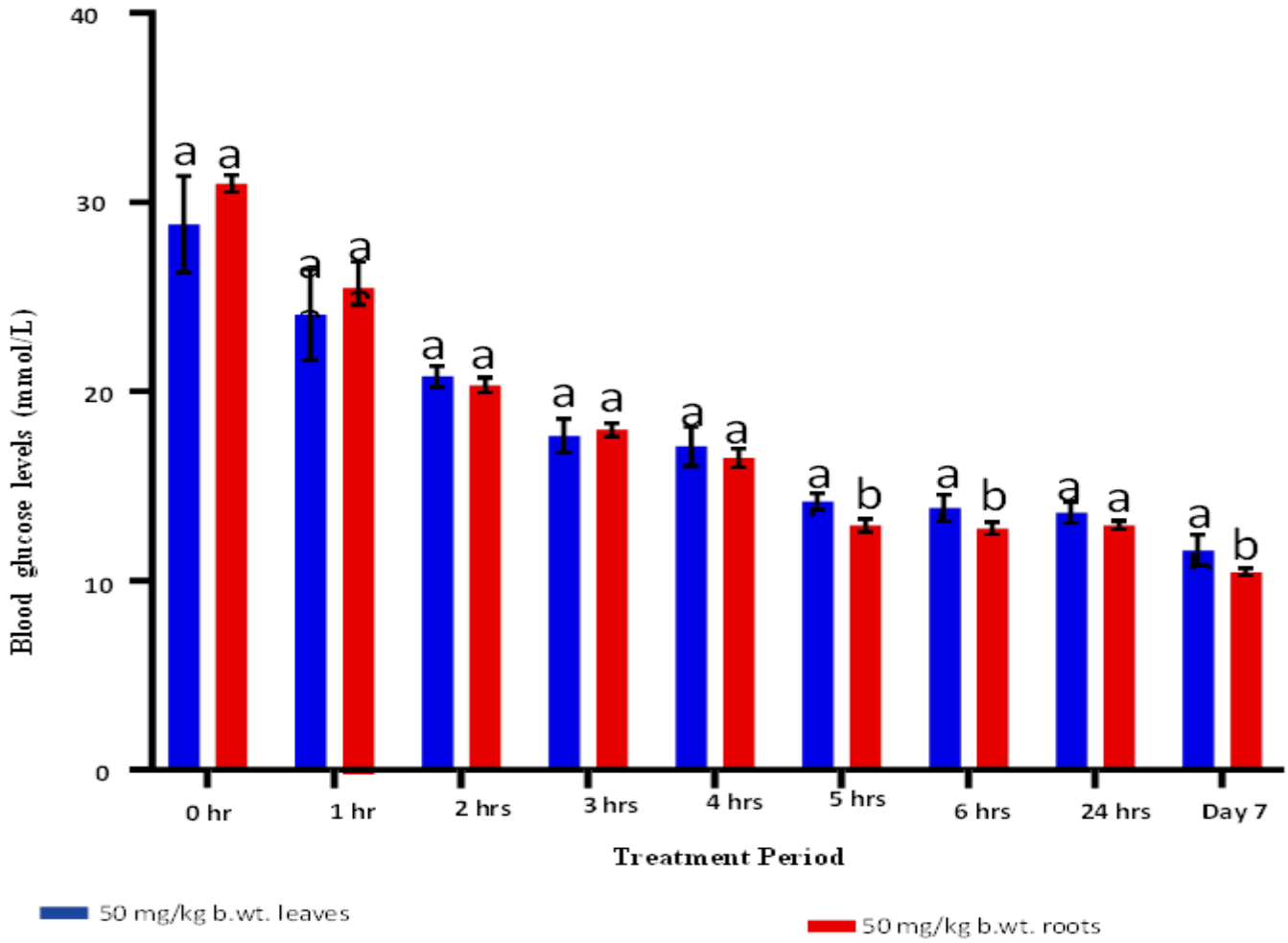

Figure 3.1: Comparison of antidiabetic effects of the leaves and root extracts of *M. barteri* at 50mg/kg b.wt. in diabetic mice. Bars with different letter at the same hour are significantly different using independent t-test ($p \leq 0.05$).

In comparison, the antidiabetic activity of *M. barteri* leaves and roots extracts at the doses of 50mg/kg. b.wt. showed no significant difference ($p>0.05$), except at hours 5,6 and day 7 ($p<0.05$; Figure 3.1)

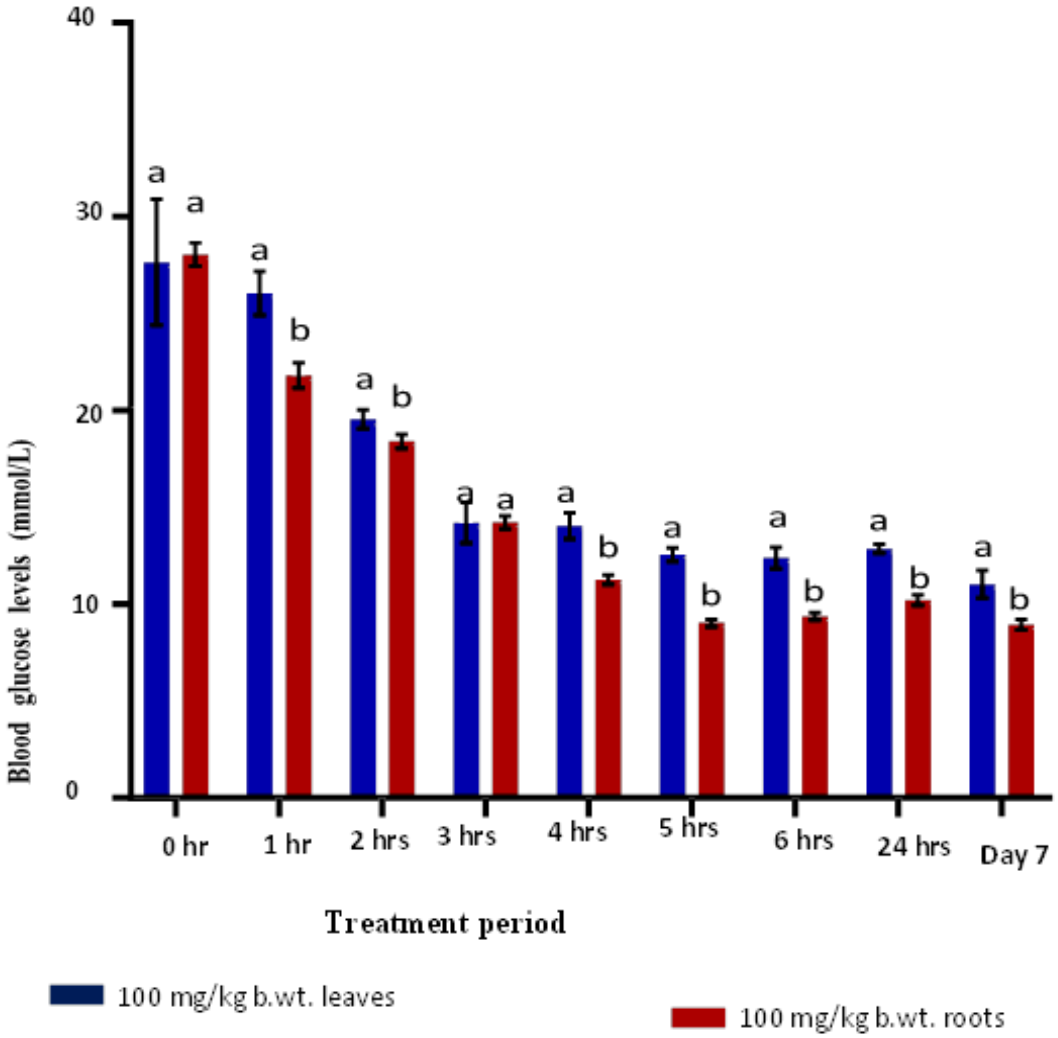

Figure 3.2: Comparison of antidiabetic effects of the leaves and root extracts of *M. barteri* at 100mg/kg b.wt. in diabetic mice. Bars with different letter at the same hour are significantly different using independent t-test ($p\leq0.05$).

The levels of blood glucose in diabetic mice administered with roots extracts of *M. barteri* at the dose of 100 mg/kg. b.wt. were significantly lower compared to those administered with leaves extracts in hours 1, 2, 4, 5, 6, 24 and day 7 ($p\leq0.05$; figure 3.2). However, the blood glucose levels in hour 0 were not significantly different ($p>0.05$).

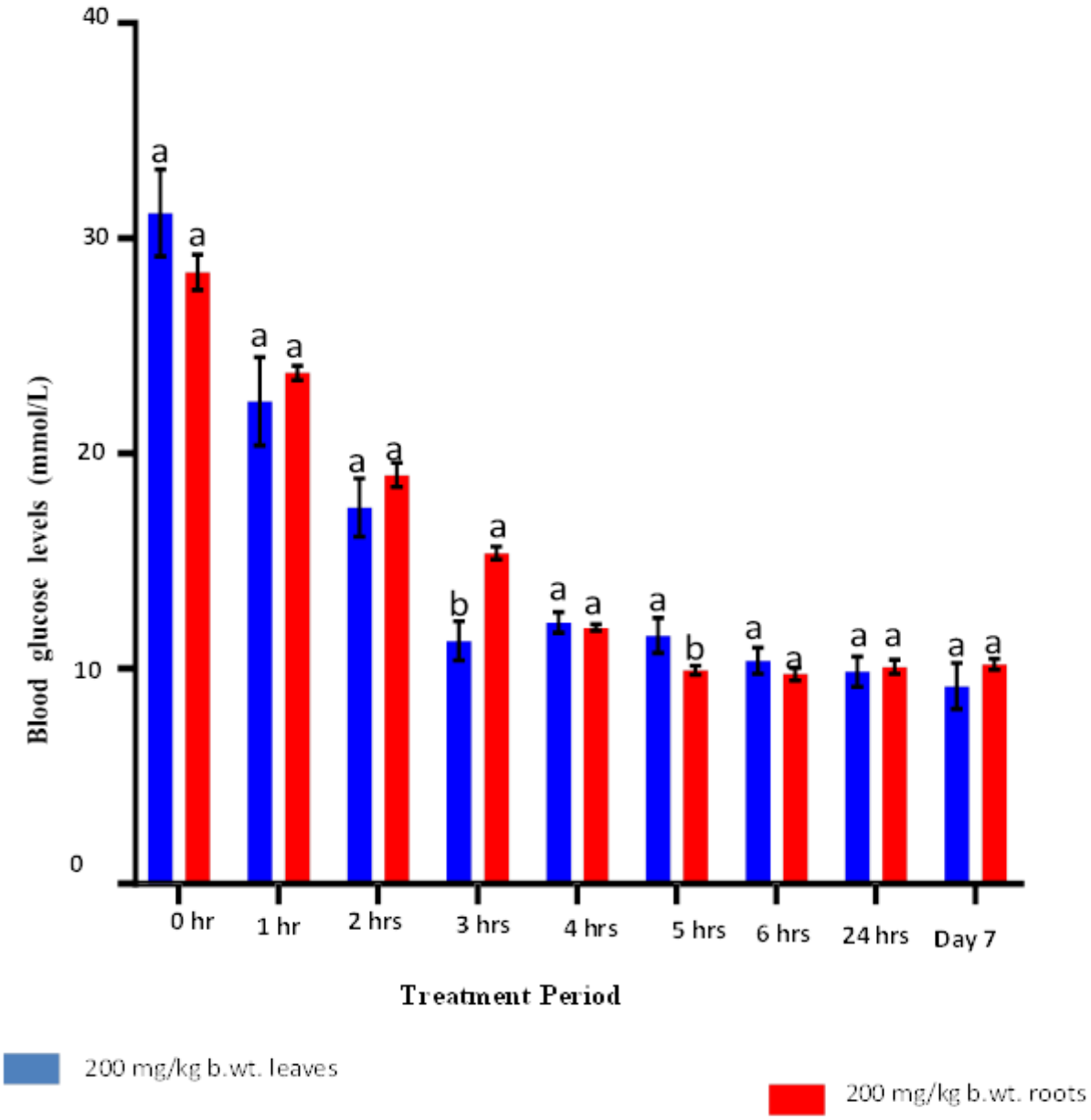

Figure 3.3: Comparison of antidiabetic effects of the leaves and root extracts of *M. barteri* at 200mg/kg b.wt. in diabetic mice. Bars with different letter at the same hour are significantly different using independent t-test ($p \leq 0.05$).

There was no significant difference in blood glucose levels of mice administered with leaves and roots extracts of *M. barteri* at the dose of 200 mg/kg b.wt. ($p>0.05$), except at the third and fifth hours of treatment ($P<0.05$; figure 3.3).

Table 6: Effects of 28 days of oral administration of *M. barteri* aqueous leaves extract on healthy mice body weight

Treatment group	Week			
	1	2	3	4
Normal control	5.09±0.35	9.73±0.82	14.84±0.64	17.63±0.79
200mg/kg.b.wt. leaves	4.58±0.49	8.03±0.53	14.15±0.79	17.36±0.76
346mg/kg.b.wt. leaves	5.23±0.61	8.83±0.71	12.26±0.61	16.46±0.38
600mg/kg.b.wt. leaves	4.32±0.51	8.52±0.63	13.01±0.82	17.02±0.57

Shown in Table 6, is the effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on the organ-to-body weight ratios of healthy mice. On the overall, the results suggest that treatment with the leaf extract did not cause any major or consistent harmful changes in the relative weights of the examined organs when compared with the normal control group. The brain weight was slightly lower in the 200 mg/kg group, slightly higher in the 346 mg/kg group, and close to the control value in the 600 mg/kg group, showing no clear dose-dependent pattern. The heart weight was reduced in the 200 mg/kg and 346 mg/kg groups but was similar to the control in the 600 mg/kg group. Kidney weights were slightly lower in all treated groups compared with the control, while lung weights remained fairly similar across all groups, indicating little or no effect of the extract on the lungs. Liver weight showed a mild reduction in the treated groups compared with the normal control, but the differences were not marked. The spleen weight appeared slightly higher in the treated groups, especially at 200 mg/kg and 346 mg/kg. In general, the absence of pronounced changes in organ-to-body weight ratios suggests that 28 days of oral administration of aqueous leaf extract of *M. barteri* may not have caused serious toxic effects on the major organs of healthy mice at the tested doses.

Table 7: Effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on healthy mice organ to body weight

Treatment group	Weight of organ					
	Brain	Heart	Kidneys	Lung	Liver	Spleen
Normal control	1.29±0.07	0.63±0.03	1.59±0.06	0.98±0.04	6.17±0.37	0.59±0.05

200mg/kg.b.wt. leaves	1.06±0.04	0.49±0.03	1.48±0.11	0.96±0.06	5.86±0.21	0.73±0.07
346mg/kg.b.wt. leaves	1.41±0.09	0.49±0.03	1.44±0.06	0.93±0.06	5.63±0.46	0.67±0.05
600mg/kg.b.wt. leaves	1.22±0.14	0.62±0.06	1.48±0.08	0.86±0.03	5.29±0.43	0.67±0.04

Table 7 presents the effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on the organ-to-body weight ratios of healthy mice. Generally, the findings show that the extract did not produce marked or severe changes in the relative weights of the organs studied when compared with the normal control group. The brain weight was slightly reduced in the 200 mg/kg group, increased in the 346 mg/kg group, and remained close to the control value in the 600 mg/kg group, indicating no consistent dose-related trend. Heart weight was lower in the 200 mg/kg and 346 mg/kg groups but was almost the same as the control in the 600 mg/kg group. Kidney weight showed a slight reduction across all treated groups compared with the control. Lung weight remained relatively stable, although a small decrease was observed at the highest dose of 600 mg/kg. Liver weight showed a gradual reduction from the control to the treated groups, with the lowest value recorded at 600 mg/kg, suggesting a mild dose-related decrease. The spleen weight was slightly higher in all treated groups than in the normal control group. Overall, the relatively small variations observed across the organ weights suggest that repeated oral administration of aqueous leaf extract of *M. barteri* for 28 days did not cause serious toxic effects on the major organs of healthy mice at the doses tested.

Table 8: Effects of 28 days of oral administration of aqueous root extract of *M. barteri* on healthy mice organ to body weight

Treatment group	Weight of organ					
	Brain	Heart	Kidneys	Lung	Liver	Spleen
Normal control	1.29±0.07	0.63±0.03	1.59±0.06	0.98±0.04	6.17±0.37	0.59±0.05
200mg/kg.b.wt. roots	1.19±0.03	0.54±0.01	1.39±0.04	0.87±0.05	5.68±0.47	0.77±0.05
346mg/kg.b.wt. roots	1.27±0.0	0.56±0.04	1.49±0.02	0.89±0.05	5.52±0.24	0.74±0.07
600mg/kg.b.wt. roots	1.22±0.08	0.60±0.02	1.59±0.06	0.93±0.07	5.11±0.10	0.75±0.05

Table 8 shows the effects of 28 days of oral administration of aqueous root extract of *M. barteri* on the organ-to-body weight ratios of healthy mice. In general, the findings indicate that the root extract did not produce marked or severe alterations in the relative weights of the organs examined when compared with the normal control group. Brain weight remained fairly close to the control across all treated groups, with only slight reductions at 200 mg/kg and 600 mg/kg, while the 346 mg/kg group was almost similar to the control. Heart weight was slightly lower in all treated groups than in the control, although the difference was less pronounced at the highest dose. Kidney weight was reduced in the 200 mg/kg and 346 mg/kg groups, but at 600 mg/kg it returned to a value similar to that of the normal control. Lung weight also showed a slight reduction in the treated groups, though the values remained relatively close to the control. Liver weight displayed a gradual decrease across the treatment groups, with the lowest value observed at 600 mg/kg, suggesting a mild dose-related reduction. Spleen weight was consistently higher in all root extract-treated groups compared with the control group. Overall, the changes observed in organ-to-body weight ratios were relatively small and did not follow a strong pattern of toxicity, suggesting that repeated oral administration of aqueous root extract of *M. barteri* for 28 days may not have caused serious adverse effects on the major organs of healthy mice at the tested doses.

Table 9: Effects of aqueous leaves extract of *M. barteri* on erythrocytes and related parameters after 28 days of oral administration

Treatment group	**Hematological parameters and indices**					
	RBC ($x10^6/\mu L$)	MCH (pg)	MCHC (g/dL)	MCV (fL)	HGB (g/dL)	RDW (fL)
Normal control	9.79 ± 0.15^a	15.72 ± 0.18^a	32.84 ± 0.28^a	49.61 ± 0.72^a	15.56 ± 0.35^a	34.02 ± 0.29^a
200mg/kg b.wt. leaves	10.20 ± 0.21^a	15.70 ± 0.15^a	33.02 ± 0.18^a	48.02 ± 0.54^a	16.16 ± 0.25^a	28.90 ± 0.35^b
346mf/kg b.wt. leaves	9.66 ± 0.27^a	15.12 ± 0.33^a	33.38 ± 0.28^a	48.26 ± 0.30^a	15.66 ± 0.25^a	28.76 ± 0.57^b
600mg/kg b.wt. leaves	9.85 ± 0.28^a	15.54 ± 0.17^a	33.30 ± 0.20^a	48.00 ± 0.62^a	15.80 ± 0.31^a	29.32 ± 0.53^b

Table 9 presents the effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on erythrocytes and related hematological parameters in healthy mice. Overall, the findings show that the leaf extract did not produce major changes in most of the red blood cell indices when compared with the normal control group. The red blood cell count (RBC), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular

volume (MCV), and hemoglobin concentration (HGB) remained relatively similar across the control and treated groups, with no statistically significant differences, as indicated by the same superscript letter "a." This suggests that the aqueous leaf extract did not adversely affect red blood cell production, hemoglobin content, or red cell size during the 28-day treatment period. However, red cell distribution width (RDW) was noticeably lower in all extract-treated groups compared with the normal control, and these values carried a different superscript letter "b," indicating a statistically significant reduction. This decrease in RDW suggests that the treated mice had less variation in red blood cell size compared with the control group. In general, the results indicate that oral administration of aqueous leaf extract of *M. barteri* for 28 days had no harmful effect on the major erythrocyte parameters and may have maintained stable red blood cell status in healthy mice, except for a significant reduction in RDW.

10. Effects of aqueous roots extract of *M. barteri* on erythrocytes and related parameters after 28 days of oral administration

Treatment group	**Hematological parameters and indices**					
	RBC ($x10^6/\mu L$)	**MCH (pg)**	**MCHC (g/dL)**	**MVC (fL)**	**HGB (g/dL)**	**RDW (fL)**
Normal control	9.79 ± 0.15^a	15.72 ± 0.18^a	32.84 ± 0.28^b	49.61 ± 0.72^a	15.56 ± 0.35^a	34.02 ± 0.29^a
200mg/kg b.wt. roots	9.74 ± 0.27^a	15.78 ± 0.20^a	33.86 ± 0.17^a	46.23 ± 0.89^a	15.68 ± 0.46^a	29.28 ± 0.62^c
346mf/kg b.wt. roots	9.60 ± 0.21^a	15.62 ± 0.16^a	33.86 ± 0.14^a	47.81 ± 1.69^a	14.98 ± 0.21^a	27.36 ± 0.25^d
600mg/kg b.wt. roots	9.55 ± 0.17^a	15.72 ± 0.13^a	33.26 ± 0.32^{ab}	45.63 ± 1.12^a	14.80 ± 0.30^a	31.48 ± 0.55^b

Table 10 presents the effects of 28 days of oral administration of aqueous root extract of *M. barteri* on erythrocytes and related hematological indices in healthy mice. Overall, the results indicate that the root extract did not cause major disruptions in most of the red blood cell parameters when compared with the normal control group. The red blood cell count (RBC), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), and hemoglobin concentration (HGB) remained relatively stable across all treated groups, showing no meaningful or consistent deviations from the control values.

However, some variations were observed in mean corpuscular hemoglobin concentration (MCHC), where the control group differed slightly from the treated groups, suggesting mild changes in hemoglobin concentration within red blood cells. The most notable changes were observed in red cell distribution width (RDW), where all treated groups showed a marked reduction compared with the control, with different levels of statistical significance indicated by the superscript letters. This reduction suggests a decrease in the variation of red blood cell size among treated animals. Overall, the findings suggest that repeated oral administration of aqueous root extract of *M. barteri* for 28 days did not adversely affect the core erythrocyte profile of healthy mice, although it produced significant and dose-related effects on RDW and minor variations in some red cell indices.

Table 11: Effects of aqueous leaves extract of *M. barteri* on platelets, differential white blood cells counts and related parameters after 28 days of oral administration.

Treatment group	**Platelets, differential white blood cells count and other hematological indices**				
	WBC ($x10^3/\mu L$)	NEU ($x10^3/\mu L$)	LYMP (g/dL)	MON ($x10^9$)	EOS ($x10^3/\mu L$)
Normal control	7.47 ± 0.44^{b}	1.95 ± 0.13^{a}	5.49 ± 0.40^{b}	0.03 ± 0.00^{a}	0.00 ± 0.00^{b}
200mg/kg b.wt. leaves	8.27 ± 0.10^{ab}	2.26 ± 0.19^{a}	5.99 ± 0.14^{ab}	0.01 ± 0.00^{b}	0.01 ± 0.00^{a}
346mg/kg b. wt. leaves	8.29 ± 0.21^{ab}	2.27 ± 0.24^{a}	6.01 ± 0.33^{ab}	0.01 ± 0.00^{b}	0.00 ± 0.00^{b}
600mg/kg b. wt. leaves	8.81 ± 0.31^{a}	1.89 ± 0.26^{a}	6.91 ± 0.08^{a}	0.02 ± 0.00^{ab}	0.00 ± 0.00^{b}

Table 11 presents the effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on platelets, differential white blood cell counts, and related hematological parameters in healthy mice. Overall, the results suggest that the extract produced mild but notable changes in some immune-related blood parameters, while others remained relatively stable. The total white blood cell (WBC) count showed a slight increase in all treated groups compared with the normal control, with the highest value observed in the 600 mg/kg group, indicating a possible dose-related stimulatory effect on immune cell production, although statistical differences were minimal between some groups as indicated by overlapping superscripts. Neutrophil (NEU) counts remained fairly consistent across all groups, suggesting no significant effect on this component of the innate immune response. Lymphocyte (LYMP) levels showed a gradual increase in the treated groups, particularly at the highest dose, which may indicate a mild enhancement of adaptive immune activity. Monocyte (MON) counts were low across all groups, with slight variations between control

and treated animals, but without a clear toxic or suppressive pattern. Eosinophil (EOS) values were very low overall, with minor fluctuations between groups, indicating no strong allergic or parasitic-type response induced by the extract. In general, the findings suggest that oral administration of aqueous leaf extract of *M. barteri* for 28 days did not produce harmful immunosuppressive effects, but rather showed mild immunomodulatory tendencies, particularly reflected in the slight increases in total WBC and lymphocyte counts at higher doses.

Table 12: Effects of aqueous roots extract of *M. barteri* on platelets, differential white blood cells counts and related parameters after 28 days of oral administration.

Treatment group	**Platelets, differential white blood cells count and other hematological indices**				
	WBC ($x10^3/\mu L$)	NEU ($x10^3/\mu L$)	LYMP (g/dL)	MON ($x10^9$)	EOS ($x10^3/\mu L$)
Normal control	7.47 ± 0.44^{a}	1.95 ± 0.13^{a}	5.49 ± 0.40^{ab}	0.03 ± 0.00^{b}	0.00 ± 0.00^{b}
200mg/kg b.wt. roots	8.18 ± 0.20^{a}	2.19 ± 0.18^{a}	5.98 ± 0.19^{a}	0.01 ± 0.00^{b}	0.00 ± 0.00^{b}
346mg/kg b.wt. roots	7.57 ± 0.34^{a}	2.86 ± 0.36^{a}	4.68 ± 0.40^{bc}	0.03 ± 0.01^{b}	0.00 ± 0.00^{b}
600mg/kg b.wt. roots	7.14 ± 0.18^{a}	2.71 ± 0.19^{a}	4.17 ± 0.21^{c}	0.26 ± 0.02^{a}	0.01 ± 0.00^{a}

Table 12 presents the effects of 28 days of oral administration of aqueous root extract of *M. barteri* on platelets, differential white blood cell counts, and related hematological indices in healthy mice. Overall, the findings indicate that the root extract produced some dose-dependent variations in immune-related blood parameters, while several other indices remained relatively stable. The total white blood cell (WBC) count showed no consistent significant change across the treated groups compared with the normal control, suggesting that overall leukocyte production was largely maintained. Neutrophil (NEU) counts were also fairly stable across all groups, indicating no marked effect on innate immune cell levels.

However, lymphocyte (LYMP) levels showed a decreasing trend with increasing doses of the root extract, particularly at 346 mg/kg and 600 mg/kg, suggesting a possible dose-related suppression of lymphocyte proportion in peripheral blood. Monocyte (MON) counts were generally low in most groups, but a notable and statistically significant increase was observed at the highest dose (600 mg/kg), indicating a possible stimulatory or reactive effect on monocyte production at higher

exposure. Eosinophil (EOS) counts remained absent or very low in most groups, with a slight increase observed only at the highest dose, although still minimal overall.

In general, the results suggest that while aqueous root extract of *M. barteri* for 28 days did not significantly alter total white blood cell counts or neutrophil levels, it produced dose-related alterations in lymphocyte and monocyte distributions, particularly at higher doses, indicating a mild immunomodulatory effect rather than overt toxicity or severe immunosuppression.

Table 13: Effects of 28 days oral administration of M. barteri leaves extract on the liver and kidney biomarkers of healthy mice

Treatment group	Effects on enzyme activity		
	ALT (U/L)	AST (U/L)	UREA (mg/dL)
Normal control	45.97±0.76a	182.60±3.40b	42.64±1.25a
200mg/kg b.wt. leaves	46.59±0.96a	188.80±2.92ab	43.58±0.63a
346mg/kg b.wt. leaves	46.62±0.59a	189.80±3.06ab	44.16±0.63a
600mg/kg b.wt. leaves	47.85±0.60a	190.60±1.96a	43.64±0.94a

Table 13 presents the effects of 28 days of oral administration of aqueous leaf extract of *M. barteri* on liver and kidney function biomarkers in healthy mice. Overall, the findings indicate that the extract did not produce marked toxic effects on hepatic or renal biochemical indices when compared with the normal control group. Alanine aminotransferase (ALT) levels remained relatively stable across all treated groups, showing only slight increases that were not statistically significant, suggesting that hepatocellular integrity was largely maintained. Aspartate aminotransferase (AST) values showed minor variations, with a slight increasing trend in the treated groups; however, most of the values overlapped statistically with the control group, indicating no clear evidence of liver damage. Urea levels, which serve as an indicator of kidney function, remained fairly consistent across all groups, with no significant differences observed between the control and treated animals.

In general, the results suggest that repeated oral administration of aqueous leaf extract of *M. barteri* for 28 days did not significantly alter liver enzyme activity or kidney function markers in healthy mice. This indicates that the extract, at the tested doses, may not exert serious hepatotoxic or nephrotoxic effects under the experimental conditions.

Table 14: Effects of 28 days oral administration of *M. barteri* roots extract on the liver and kidney biomarkers of healthy mice

Treatment group	Effects on enzyme activity		
	ALT (U/L)	AST (U/L)	UREA (mg/dL)
Normal control	45.97±0.76	182.60±3.40	42.64±1.25
200mg/kg b.wt. roots	46.59±0.96	188.80±2.92	43.58±0.63
346mg/kg b.wt. roots	46.20±0.59	189.80±3.06	44.16±0.63
600mg/kg b.wt. roots	47.85±0.60	190.60±1.96	43.64±0.69

Table 14 presents the effects of 28 days of oral administration of aqueous root extract of *M. barteri* on liver and kidney function biomarkers in healthy mice. Overall, the findings show that the root extract did not cause significant or clinically relevant alterations in the biochemical indices of hepatic and renal function when compared with the normal control group. Alanine aminotransferase (ALT) levels remained relatively stable across all treated groups, with only slight increases observed at higher doses, suggesting that there was no clear evidence of hepatocellular injury. Aspartate aminotransferase (AST) values also showed a mild upward trend in the treated groups compared with the control, but the differences were not pronounced enough to indicate liver toxicity under the experimental conditions. Urea levels, which reflect kidney function, showed minimal variation across all groups, with values remaining close to those of the control group, indicating that renal function was largely unaffected by the treatment.

In general, the results suggest that repeated oral administration of aqueous root extract of *M. barteri* for 28 days did not significantly disrupt liver enzyme activity or kidney function markers in healthy mice. This indicates that the extract, at the doses tested, may not exert notable hepatotoxic or nephrotoxic effects in healthy animals under the conditions of this study.

4. Discussion

This study evaluated the hypoglycemic activity and safety profile of aqueous leaf and root extracts of Macaranga barteri in Swiss albino mice. The blood glucose levels of Swiss albino mice increased markedly following intraperitoneal administration of alloxan monohydrate at a dose of 186.9 mg/kg body weight. Alloxan monohydrate is a glucose analogue that induces hyperglycemia by selectively causing necrosis of pancreatic β-cells [35]. Consequently, alloxan-induced diabetes has been widely recognized as a suitable experimental model for studying diabetes mellitus [35].

In the present study, blood glucose levels in alloxan-induced diabetic mice were approximately three to four times higher than those observed in the normal control group.

Oral administration of the aqueous leaf and root extracts of *M. barteri* significantly reduced blood glucose levels in alloxan-induced diabetic mice. These findings are consistent with previous reports demonstrating the hypoglycemic effects of medicinal plant extracts [14][36]. The antidiabetic activity of *M. barteri* was comparable to that of glibenclamide, the standard reference drug. Among the leaf extract-treated groups, the 200 mg/kg body weight dose produced the greatest reduction in blood glucose levels compared with the 50 mg/kg and 100 mg/kg doses. In contrast, the root extract administered at 100 mg/kg body weight demonstrated a greater glucose-lowering effect than the 50 mg/kg and 200 mg/kg doses. Overall, both the leaf and root extracts exhibited hypoglycemic effects comparable to glibenclamide, indicating that *M. barteri* possesses significant antidiabetic potential.

The leaf and root extracts of *M. barteri* exhibited marked hypoglycemic activity after seven days of treatment, with no statistically significant difference observed between the two extracts. This finding suggests that either the leaves or the roots of the plant may be effectively utilized in the management of hyperglycemia. Furthermore, the hypoglycemic effect of the leaf extract at 200 mg/kg body weight was comparable to that of the root extract at 100 mg/kg body weight. These effects may be attributed to the presence of bioactive phytochemicals such as alkaloids, flavonoids, terpenes, saponins, steroids, and glycosides, which have previously been reported to possess hypoglycemic properties [37][38][39]. Previous studies have also demonstrated the therapeutic potential of the leaves and stem bark of *M. barteri* [12][16][21]. However, to the best of our knowledge, no previous study has specifically investigated the antidiabetic activity of the aqueous leaf and root extracts of *M. barteri*.

The antidiabetic properties of numerous medicinal plants have been scientifically validated. For instance, oral administration of aqueous extracts from the aerial parts of *Artemisia herba* at a dose of 390 mg/kg body weight significantly reduced blood glucose levels and prevented an increase in glycosylated hemoglobin in diabetic rats after four weeks of treatment [40], Similarly, a research study [41] reported that oral administration of *Urtica massaica* extracts at different doses produced hypoglycemic effects comparable to those of glibenclamide. Plant-derived phytochemicals such as tannins, saponins, flavonoids, steroids, and glycosides have also been shown to exert hypoglycemic effects in diabetic animal models [38][42]. Likewise, [14] reported that administration of a combination of 200 mg turmeric powder and 200 mg garlic powder to 35 hypoglycemic patients

was more effective in reducing both fasting and postprandial blood glucose levels than 5 mg of glibenclamide.

The hypoglycemic effects of the aqueous extracts of *M. barteri* may be mediated through several mechanisms. These may include enhanced glucose utilization, stimulation of insulin secretion, or increased cellular glucose uptake, all of which contribute to lowering blood glucose levels. The extracts may also stimulate the regeneration or activation of pancreatic β-cells within the islets of Langerhans, thereby increasing serum insulin levels and reducing blood glucose concentrations [43][44]. Other possible mechanisms include enhanced insulin secretion from residual or regenerated β-cells [45], improved insulin sensitivity [43], reduced intestinal absorption of dietary carbohydrates and disaccharides, and increased peripheral glucose utilization through GLUT-4 (insulin-dependent glucose transporter) activation [46].

Interestingly, the higher dose of the aqueous root extract (200 mg/kg body weight) produced a lower hypoglycemic effect than the 100 mg/kg dose. This observation may be attributed to the higher concentration of active phytoconstituents at the larger dose, which may have delayed absorption across the gastrointestinal mucosa, thereby reducing the rate of glucose-lowering activity.

The extracts did not produce a significant reduction in blood glucose levels during the first few hours following administration. However, significant reductions became evident from the second and third hours and continued through the sixth hour, twenty-fourth hour, and seventh day of treatment. This delayed onset of action may suggest that the active constituents were slowly absorbed or required metabolic biotransformation before exerting their hypoglycemic effects. Nevertheless, intraperitoneal administration of the leaf and root extracts may potentially produce greater hypoglycemic activity because of their direct inhibitory effects on glucose transporters located in the peritoneal mesothelial cells, which regulate glucose absorption across the peritoneal cavity [47].

Following the 28-day toxicity study, it was expected that treated animals would gain body weight at a rate similar to the normal control group. The relatively slower changes in body weight observed among extract-treated animals may be attributed to phytochemicals such as alkaloids, saponins, tannins, steroids, coumarins, flavonoids, and other phenolic compounds. These phytochemicals are

known to influence body weight through regulation of energy expenditure, appetite suppression, enhanced satiety, and inhibition of fat and glucose absorption [48][49].

The measurable endpoints of toxicological studies include pharmacological, biochemical, and pathological alterations that may occur either quantitatively or qualitatively. Toxicity may also manifest as quantal responses, including mortality or loss of consciousness [50]. Numerous biomarkers are used to assess toxicity, including serum enzymes released following organ injury, alterations in urinary constituents, changes in enzyme activities, and pathological abnormalities detected at gross, microscopic, and subcellular levels [27]. In the present study, oral administration of the leaf and root extracts of *M. barteri* did not produce any significant increase in kidney weight compared with the normal control group, suggesting the absence of renal toxicity.

Hematological parameters provide important information regarding blood composition and reticuloendothelial function and are therefore valuable indicators for evaluating the toxicity of exogenous substances, including medicinal plant extracts and pharmaceutical agents. Hematological assessment is particularly important because alterations in these parameters often provide reliable predictors of human toxicity based on animal studies [51][52]. The findings of this study showed that oral administration of both the leaf and root extracts had no significant effect on red blood cell count, hemoglobin concentration, or related erythrocytic indices. This observation may indicate that the extracts neither stimulated nor inhibited erythropoietin synthesis or other humoral regulators involved in erythropoiesis [52]. While red blood cell count and hemoglobin concentration reflect the total red blood cell population, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) provide information on individual erythrocytes. The absence of significant alterations in these parameters suggests that the extracts did not affect red blood cell morphology, osmotic fragility, or hemoglobin incorporation. Consequently, the oxygen-carrying capacity of the erythrocytes remained unaffected, indicating that *M. barteri* does not possess anemic potential. These findings are consistent with previous reports on hematological markers of in vivo toxicity [51].

White blood cells and their differential counts play critical roles in immune function. Neutrophils are primarily involved in phagocytosis and the elimination of bacteria, cellular debris, and foreign particles. Lymphocytes, on the other hand, are responsible for antigen recognition, differentiation, functional maturation, adaptive immune responses, and the establishment of immunological memory [27].

The liver and kidneys are essential organs involved in metabolism and detoxification. The liver plays a central role in the biotransformation of xenobiotics, whereas the kidneys are primarily responsible for the elimination of drugs and their metabolites, making both organs susceptible to toxic injury from exogenous substances [53]. Therefore, evaluating the effects of *M. barteri* extracts on these organs was essential.

Serum transaminases, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are widely recognized biomarkers of hepatic injury. Damage to hepatocytes results in increased serum concentrations of these enzymes. AST is present in both the cytoplasm and mitochondria and is found in several tissues, including the liver, kidneys, heart, and brain. Tissue injury causes AST to leak into the circulation, making it an early indicator of cellular damage [27]. In contrast, ALT is localized predominantly in the liver and is considered a more specific marker of hepatic injury.

In the present study, oral administration of the leaf and root extracts of *M. barteri* did not significantly alter serum AST, ALT, or urea levels, indicating that the extracts did not produce detectable liver or kidney toxicity under the conditions of this study.

Overall, the findings of this study scientifically support the traditional use of *M. barteri* in the management of diabetes mellitus. Following well-designed clinical studies in humans to establish its safety and efficacy, either the leaves or roots of *M. barteri* may be considered as potential monotherapy for the management of diabetes mellitus.

5. Conclusion

The present study demonstrated that aqueous leaf and root extracts of Macaranga barteri possess significant in vivo hypoglycemic activity in alloxan-induced diabetic Swiss albino mice. Both extracts reduced elevated blood glucose levels at oral doses of 50, 100, and 200 mg/kg body weight, with effects comparable to glibenclamide. The leaf extract showed the strongest activity at 200 mg/kg body weight, whereas the root extract was most active at 100 mg/kg body weight. In addition, repeated oral administration of the extracts for 28 days did not produce major adverse effects on body weight, organ-to-body weight ratios, hematological indices, or biochemical markers of liver and kidney function. These findings provide scientific support for the traditional use of M. barteri in the management of hyperglycemia and suggest that both the leaves and roots may serve as potential sources of antidiabetic agents. Further studies are required to isolate the bioactive

compounds, clarify their mechanisms of action, and establish their safety and efficacy in human subjects.

Acknowledgements

The authors sincerely acknowledge the National Phytotherapeutic Research Centre, Kenyatta University, Nairobi, for providing the facilities and technical support required to carry out this study.

Authors' Contributions

Fayia Randolph Samukai contributed to the conception and design of the study, conducted the experimental work, collected and analyzed the data, interpreted the findings, and prepared the initial manuscript draft. Nicholas K. Gikonyo contributed to the study design, supervised the experimental work, participated in data interpretation, and reviewed the manuscript draft. Michael A. Odeniyi contributed to the experimental design and manuscript development. J. Samuel Kamanda contributed to manuscript review, scientific refinement, and final editing of the article.

Funding

This research was funded by the African Union Commission through a fully funded scholarship programme.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

Ethical Approval

Ethical approval for the study was obtained from the relevant institutional ethics and animal care committees before commencement of the research.

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54. Correction: The phrase "In Syria Studies (Vol. 7, No. 1)" is a reference manager error and has been removed.