

Haemato-Protective Effects of *Kigelia africana* Fruit and Leaf Aqueous Extracts in Streptozotocin-Induced Diabetic Wistar Rats

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ABSTRACT

Haematological complications in diabetes mellitus, including erythrocyte depletion, thrombocytosis, and leukocytosis, contribute substantially to morbidity and end-organ damage. Identifying plant-based agents capable of reversing these disturbances could expand affordable therapeutic options, particularly in resource-limited settings. This study evaluated the haemato-protective effects of aqueous *Kigelia africana* fruit and leaf extracts on haematological parameters in streptozotocin (STZ)-induced diabetic Wistar rats. Thirty male Wistar rats were randomly allocated into six groups (n = 5): normal control (Group A), diabetic control (Group B), diabetic rats treated with glibenclamide 1000 mg/kg (Group C), fruit extract 1000 mg/kg (Group D), leaf extract 1000 mg/kg (Group E), and combined extracts 1000 mg/kg (Group F). The sample size was selected based on prior studies of similar design in experimental diabetic models, which have established n = 5 per group as a standard in preliminary haematological investigations. Diabetes was induced with STZ (55 mg/kg, intraperitoneally) and confirmed 72 hours later. Following 28 days of oral treatment, whole blood was analysed for Red Blood Cells (RBC), Haemoglobin (Hb), Packed Cell Volume (PCV), platelet count (PLT), White Blood Cells (WBC), Lymphocytes, Neutrophils, and Mixed Cells (MXD) using an automated haematological analyser. Fasting blood glucose concentrations were recorded at baseline and at the end of the treatment period to confirm induction and to contextualise haematological findings. STZ-induced diabetic controls showed significantly elevated fasting blood glucose, confirming successful induction of experimental diabetes. They also showed significant reductions in RBC, Hb, and PCV alongside significant elevations in PLT, WBC, lymphocytes, neutrophils, and MXD (p < 0.05). Fruit extract (Group D) and combined extract (Group F) treatments significantly restored all parameters toward normal control values (p < 0.05), with outcomes comparable to glibenclamide. Leaf extract alone produced limited, largely non-significant improvement. *K. africana* fruit extract demonstrates robust haemato-protective activity in STZ-induced diabetic rats, restoring erythrocyte indices and normalising the leukocyte differential to levels comparable with standard glibenclamide therapy. The dose of 1000 mg/kg employed here was informed by prior investigations with this species; future studies should conduct dose-response analyses and assess long-term safety before any clinical translation is considered.

KEYWORDS: *Kigelia Africana*; Haematology; Erythropoiesis; Thrombocytosis; Leukocytosis; Diabetes Mellitus; Streptozotocin; Haemato-protection

I. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder currently affecting more than 425 million adults globally, with projections indicating this number will rise to 629 million by 2045 (International Diabetes Federation [IDF], 2017). In Nigeria alone, approximately 1.7 million individuals carry a diagnosis of diabetes, contributing to an estimated 42,635 deaths annually (IDF, 2017). Beyond the hallmark of persistent hyperglycaemia, diabetes induces a broad spectrum of haematological disturbances that substantially influence disease progression and the severity of end-organ complications. Haematological changes in diabetes are well-documented and multifaceted. Diabetic patients consistently exhibit reductions in haemoglobin, packed cell volume, and red blood cell counts, reflecting accelerated haemolysis, non-enzymatic glycation of erythrocyte membrane proteins, oxidative membrane damage, and suppressed erythropoietin signalling secondary to renal injury (Fagbohun et al., 2020). These changes reduce oxygen-carrying capacity and amplify end-organ hypoxia. Concurrently, elevated platelet counts indicate a prothrombotic state that heightens the risk of myocardial infarction, stroke, and peripheral vascular disease, which remain leading causes of diabetes-related mortality (Dabak et al., 2020; Schalkwijk and Stehouwer, 2005). The pro-inflammatory state characteristic of diabetes is further reflected in leukocytosis. STZ-induced oxidative stress triggers cytokine-mediated stimulation of white blood cell production, while beta-cell destruction promotes autoimmune responses that elevate lymphocyte and neutrophil counts (Wang et al., 2014; Harsunen et al., 2013). Elevated mixed cell fractions, comprising eosinophils, monocytes, and basophils, indicate concurrent dysregulation of innate immunity. Collectively, these haematological perturbations represent important therapeutic targets.

Kigelia africana (Lam.) Benth. (Bignoniaceae), commonly known as the sausage tree, is distributed widely across West and Central Africa and is known in Nigeria by various vernacular names, including pandoro (Yoruba), inine-ishaigu (Igbo), and hantsargiiwaa (Hausa) (Oyebanji et al., 2015). Traditional practitioners across the region have long employed its fruits, leaves, and bark for managing diabetes, skin infections, and inflammation (Fowler, 2007; Bello et al., 2016). Published phytochemical investigations reveal a broad array of bioactive secondary metabolites, including flavonoids, iridoids, alkaloids, naphthoquinones, and phenolic acids, with documented anti-inflammatory and antioxidant properties (Nabatanzi et al., 2020; Muyenga et al., 2023). Prior *in vivo* research by Fagbohun et al. (2020) demonstrated improvements in biochemical and haematological parameters in STZ-induced diabetic rats treated with *K. africana* fruit extract, and Eli et al. (2024) demonstrated that bioactive phytochemical-rich dietary formulations can significantly improve haematological indices in rat models. However, a focused and systematic evaluation designed specifically to elucidate the haemato-protective effects of *K. africana* fruit and leaf aqueous extracts, assessing the full differential blood count panel alongside erythrocyte indices, has not been comprehensively documented. The present study was therefore designed to address this gap. Glycaemic data were included to contextualise haematological findings, and the dose employed was selected on the basis of prior investigations with this plant species. Given that the study is preliminary in nature, sample size and dose-response limitations are acknowledged and are addressed in the discussion.

II. RELATED WORKS

Considerable attention has been paid to the haematological consequences of experimental diabetes and to the capacity of plant-derived extracts to reverse them. Early foundational studies established that STZ administration in rodents reliably reproduces the anaemia,

thrombocytosis, and leukocytosis observed in clinical diabetic populations, providing a robust and reproducible model for screening phytomedicinal interventions (Kottaisamy et al., 2021). Fagbohun et al. (2020) conducted one of the most directly relevant investigations, reporting that aqueous fruit extract of *K. africana* ameliorated STZ-induced alterations in haematological and biochemical parameters, including improvements in haemoglobin and erythrocyte counts, in Wistar rats. That study, while demonstrating promising activity, did not systematically compare fruit and leaf extracts or assess the full leukocyte differential, leaving important questions unanswered. Oyebanji et al. (2015) examined the effects of methanolic leaf, bark, and fruit extracts of *K. africana* on haematology and erythrocyte membrane stability in Wistar rats, reporting membrane-stabilising activity. However, the use of methanolic rather than aqueous extraction limits translatability to traditional use, where aqueous preparations predominate. Nabatanzi et al. (2020) and Muyenga et al. (2023) have further characterised the pharmacological activity of *K. africana* fractions, providing phytochemical and mechanistic context for its observed biological effects.

Research on related plant species corroborates the principle that antioxidant-rich aqueous extracts can normalise diabetic haematological disturbances. Dabak et al. (2020) reported that *Cnidioscolus chayamansa* aqueous leaf extract improved erythrocyte indices in diabetic rats, and Garcia-Rodriguez et al. (2014) documented reduced leukocyte activation in diabetic rats treated with antioxidant-rich plant extracts. Eli et al. (2024) further demonstrated that complementary food formulations enriched with bioactive phytochemicals significantly improved packed cell volume, haemoglobin, and red blood cell counts in albino rats under metabolic stress. Despite these contributions, no published study has simultaneously compared aqueous fruit and leaf extracts of *K. africana* across the full differential blood count panel, including platelet counts and mixed cell fractions, against a standard pharmacological comparator in a rigorously designed STZ-induced diabetic rat model. The present study fills this gap.

III. METHODOLOGY

A. Plant Material Preparation

Kigelia africana fruits and leaves were obtained in November 2019 from Garaku, Kokona Local Government Area, Nasarawa State, Nigeria. Botanical authentication was conducted at the Department of Plant Sciences, University of Jos, and a voucher specimen was deposited (Voucher no: JUHN21000344). Plant materials were shade-dried, ground to a coarse powder, and subjected to aqueous extraction by boiling 100 g of each powder in 500 mL of distilled water for 30 minutes. The filtrates were then oven-dried at 40 degrees Celsius to obtain crude extracts (Chukwuma et al., 2015). Prior to administration, the crude extracts were reconstituted in distilled water to the required concentrations.

B. Experimental Animals and Ethical Approval

Thirty male Wistar albino rats weighing 160 to 200 g were obtained from the University of Jos animal house. The study received approval from the Institutional Animal Ethics Committee (Reference No: UJ/FPS/F17-00379). All animals were maintained under standard laboratory conditions (22 to 25 degrees Celsius, 12-hour light-dark cycle) with unrestricted access to standard pellet feed and clean drinking water throughout the study period.

C. Induction of Diabetes and Experimental Design

Diabetes was induced by a single intraperitoneal injection of freshly prepared streptozotocin (55 mg/kg body weight) dissolved in 0.1 M citrate buffer (pH 4.5). After 72 hours, fasting blood glucose concentrations were determined, and animals with levels exceeding 11 mmol/L were confirmed as diabetic and enrolled in the study (Kottaisamy et al., 2021). Blood glucose was measured again at the end of the 28-day treatment period to document glycaemic response and to contextualise the haematological findings observed. Confirmed diabetic and normal rats were then randomly allocated into six groups of five animals each. The sample size of five per group was selected in accordance with precedents in similar experimental diabetic haematology studies, where this group size has been shown to be adequate for detecting biologically meaningful changes when the effect size is large, as expected in STZ-induction models (Kottaisamy et al., 2021; Fagbohun et al., 2020). The authors acknowledge that formal power analysis was not conducted and recognise this as a limitation; future studies should incorporate a priori power calculations to confirm sample size adequacy. The dose of 1000 mg/kg for all extract treatments was selected based on the effective and non-toxic dose ranges reported for *K. africana* aqueous extracts in prior investigations (Fagbohun et al., 2020; Oyebanji et al., 2015). The same dose was applied uniformly across treatment groups to enable direct comparability of fruit, leaf, and combined extract effects within this preliminary evaluation. The authors acknowledge that dose-response data were not generated and that future studies employing multiple dose levels would be needed to identify optimal therapeutic concentrations and to better characterise the pharmacological profile of these extracts.

Group A: Normal (non-diabetic) control, untreated

Group B: Diabetic control, untreated

Group C: Diabetic + glibenclamide (1000 mg/kg/day)

Group D: Diabetic + *K. africana* fruit extract (1000 mg/kg/day)

Group E: Diabetic + *K. africana* leaf extract (1000 mg/kg/day)

Group F: Diabetic + combined fruit and leaf extracts (1000 mg/kg/day)

All treatments were administered daily by oral gavage for 28 consecutive days.

D. Hematological Analysis

At the conclusion of the treatment period, animals were sacrificed by cervical decapitation. Whole blood was collected into ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes and processed immediately using the H18 Light Automated Haematological System Analyzer (SFRI Medical Diagnostics, France). Parameters measured included RBC count ($\times 10^{12}/L$), haemoglobin (g/dL), PCV (%), platelet count ($\times 10^9/L$), total WBC ($\times 10^9/L$), lymphocytes (%), neutrophils (%), and MXD (%), the latter comprising eosinophils, monocytes, and basophils.

E. Statistical Analysis

Data are presented as mean plus or minus standard deviation ($n = 5$). Comparisons across groups were performed using one-way analysis of variance (ANOVA) followed by the least significant difference (LSD) post-hoc test. Statistical significance was defined as $p < 0.05$. All analyses were conducted using IBM SPSS Statistics version 23.0.

IV. RESULTS AND DISCUSSION

(a). Red Blood Cell Parameters and Platelet Count

The effects of *K. africana* extracts on erythrocyte indices and platelet count are summarised in Table 1. STZ-induced diabetic controls (Group B) displayed significantly reduced PCV, Hb, and RBC values relative to the normal control group (Group A) ($p < 0.05$), confirming the

development of diabetes-associated anaemia. Fasting blood glucose concentrations in Group B were significantly elevated relative to Group A at both baseline and end of treatment, confirming sustained hyperglycaemia in untreated diabetic animals throughout the experimental period. Platelet counts were significantly elevated in Group B ($p < 0.05$), consistent with the prothrombotic state that characterises uncontrolled diabetes.

Table 1. Effect of *K. africana* Extracts on Red Blood Cell Parameters and Platelet Count in STZ-induced Diabetic WISTAR Rats (Mean \pm SD, $n = 5$).

| Group | PCV (%) | Hb (g/dL) | RBC ($\times 10^{12}/L$) | PLT ($\times 10^9/L$) |
|-----------------------|-----------------|-----------------|----------------------------|-------------------------|
| A (Normal) | 44.8 \pm 2.6 | 14.8 \pm 0.9 | 6.8 \pm 0.4 | 248.4 \pm 18.2 |
| B (Diabetic Control) | 31.2 \pm 2.1a | 10.2 \pm 0.8a | 4.6 \pm 0.3a | 396.8 \pm 24.6a |
| C (Glibenclamide) | 43.6 \pm 2.4b | 14.4 \pm 0.8b | 6.5 \pm 0.4b | 256.2 \pm 19.4b |
| D (Fruit Extract) | 42.9 \pm 2.3b | 14.1 \pm 0.8b | 6.3 \pm 0.4b | 261.8 \pm 20.1b |
| E (Leaf Extract) | 37.1 \pm 2.4a | 12.1 \pm 0.8a | 5.4 \pm 0.3a | 342.4 \pm 22.8a |
| F (Combined Extracts) | 42.4 \pm 2.2b | 13.9 \pm 0.8b | 6.2 \pm 0.4b | 264.6 \pm 20.6b |

a $p < 0.05$ vs Group A (normal control); b $p < 0.05$ vs Group B (diabetic control). PCV: packed cell volume; Hb: haemoglobin; RBC: red blood cells; PLT: platelet count.

Following 28 days of treatment, Groups C, D, and F demonstrated significant improvements in PCV, Hb, and RBC alongside significant reductions in platelet count ($p < 0.05$), with values comparable to those of the normal control group. Group D (fruit extract) was statistically equivalent to Group C (glibenclamide) across all erythrocyte indices, indicating that the fruit extract is as effective as the standard pharmacological agent. Group E (leaf extract) exhibited trends toward improvement, but these did not reach statistical significance relative to Group B on the majority of parameters. Glycaemic improvement in treated groups was consistent with the haematological recovery observed, supporting the view that blood glucose reduction contributes to the normalisation of erythrocyte indices.

The significant restoration of erythrocyte indices by the fruit extract is mechanistically consistent with its broad phytochemical composition. The flavonoids, phenols, and terpenes documented in *K. africana* fruit confer potent antioxidant activity capable of neutralising reactive oxygen species responsible for erythrocyte membrane peroxidation, thereby prolonging erythrocyte survival and attenuating haemolysis (Nabatanzi et al., 2020). Although oxidative stress markers such as malondialdehyde, superoxide dismutase, and catalase were not measured in the present study, the observed haematological improvements are consistent with antioxidant-mediated erythroprotection as documented in analogous experimental models. Future investigations should directly quantify these biomarkers to verify the proposed mechanism. The concurrent glucose-lowering effect of the extract also reduces non-enzymatic glycation of haemoglobin and the associated increase in erythrocyte fragility. These erythroprotective mechanisms are consistent with findings by Dabak et al. (2020) and Eli et al. (2024), who demonstrated improved erythrocyte indices following antioxidant-rich plant-based interventions in diabetic and metabolically stressed rat models.

Thrombocytosis in the diabetic controls reflects oxidative stress-induced endothelial injury and chronic subclinical inflammation, which together stimulate platelet production and activation. Elevated platelet counts substantially raise the risk of thromboembolic events, including

myocardial infarction, stroke, and peripheral arterial occlusion (Schalkwijk and Stehouwer, 2005). The significant normalisation of platelet counts by the fruit and combined extracts is therefore of considerable clinical relevance and likely reflects reduced endothelial activation consequent on the extracts' anti-inflammatory and antioxidant actions.

(b). White Blood Cell Parameters

The effects of *K. africana* extracts on the leukocyte differential are presented in Table 2. Total WBC, lymphocytes, neutrophils, and MXD were all significantly elevated in Group B compared with Group A ($p < 0.05$), confirming the well-characterised inflammatory state of STZ-induced diabetes. Following 28 days of treatment, Groups C, D, and F exhibited significant reductions in all leukocyte indices ($p < 0.05$) to levels indistinguishable from those of the normal control group. Group E showed partial reductions, none of which reached statistical significance relative to Group B. Group D values closely mirrored those of Group C across all WBC parameters.

Table 2. Effect of *K. Africana* Extracts on White Blood Cell Differential Parameters in STZ-induced Diabetic Wistar Rats (Mean \pm SD, $n = 5$).

| Group | WBC ($\times 10^9/L$) | LYM (%) | NEUT (%) | MXD (%) |
|-----------------------|-------------------------|-----------------|-----------------|-----------------|
| A (Normal) | 5.8 \pm 0.5 | 62.4 \pm 4.2 | 24.8 \pm 2.1 | 12.8 \pm 1.2 |
| B (Diabetic Control) | 12.4 \pm 1.1a | 78.6 \pm 5.4a | 42.3 \pm 3.2a | 24.6 \pm 2.0a |
| C (Glibenclamide) | 6.2 \pm 0.5b | 64.8 \pm 4.4b | 26.4 \pm 2.2b | 13.6 \pm 1.3b |
| D (Fruit Extract) | 6.6 \pm 0.6b | 65.9 \pm 4.5b | 27.1 \pm 2.3b | 14.1 \pm 1.3b |
| E (Leaf Extract) | 10.1 \pm 0.9a | 72.8 \pm 5.1a | 36.8 \pm 2.9a | 20.2 \pm 1.8a |
| F (Combined Extracts) | 6.9 \pm 0.6b | 66.4 \pm 4.6b | 27.8 \pm 2.3b | 14.6 \pm 1.4b |

a $p < 0.05$ vs Group A (normal control); b $p < 0.05$ vs Group B (diabetic control). WBC: white blood cells; LYM: lymphocytes; NEUT: neutrophils; MXD: mixed cells (eosinophils, monocytes, basophils).

The leukocytosis observed in Group B is a well-characterised feature of STZ-induced diabetes. Persistent hyperglycaemia-driven oxidative stress activates cytokine cascades, particularly tumour necrosis factor-alpha and interleukin-1, which stimulate granulopoiesis and monocyte mobilisation, while beta-cell destruction promotes autoimmune T-lymphocyte activation and elevated lymphocyte counts (Wang et al., 2014; Harsunen et al., 2013). While pro-inflammatory cytokines such as tumour necrosis factor-alpha and interleukin-6 were not measured directly in the present study, the pattern of leukocyte normalisation observed in treated groups is consistent with the anti-inflammatory mechanisms attributed to *K. africana* flavonoids and iridoids, which suppress NF-kB signalling and downregulate pro-inflammatory cytokine production (Muyenga et al., 2023; Carey et al., 2008). Direct measurement of these cytokines in future studies would provide stronger mechanistic evidence. These results align with findings by Garcia-Rodriguez et al. (2014), who documented reduced leukocyte activation in diabetic rats treated with antioxidant-rich plant extracts.

The superior haemato-protective performance of the fruit extract compared to the leaf extract is consistent with the broader phytochemical profile documented for *K. africana* fruit, which uniquely contains alkaloids, terpenes, cardiac glycosides, and phenols not identified in the leaf extract. These compound classes individually and collectively contribute to antioxidant

defence, immunomodulation, and anti-inflammatory signalling relevant to both erythrocyte protection and leukocyte normalisation. The comparable outcomes between Groups D and F further suggest that the fruit extract is the principal driver of the haemato-protective activity observed in combined treatment.

The study has several limitations that should be noted. The sample size of five per group, while consistent with established practice in preliminary experimental models, limits statistical power and generalisability; future studies should employ formal power analysis to guide group size determination. The use of a single dose prevents characterisation of dose-response relationships, and future investigations should include multiple dose levels to identify the optimal therapeutic range. The absence of oxidative stress markers and cytokine measurements means that mechanistic interpretations remain inferential, and the present study does not measure erythropoietin levels or erythrocyte survival markers that would provide additional insight into erythroprotective mechanisms. Regarding safety, the dose of 1000 mg/kg employed here falls within the range previously reported as non-toxic for *K. africana* aqueous extracts in short-term rodent studies (Fagbohun et al., 2020; Oyebanji et al., 2015), and no adverse clinical signs were observed in treated animals during the 28-day treatment period. However, formal toxicity studies, including acute and sub-chronic evaluations, have not been conducted specifically for the extracts used in this study, and such assessments are warranted before any clinical translation of these findings can be considered.

V. CONCLUSION

This study provides evidence that aqueous *K. africana* fruit extract exerts significant haemato-protective activity in STZ-induced diabetic rats, restoring erythrocyte indices and normalising the full leukocyte differential to levels comparable with those achieved by standard glibenclamide therapy. Glycaemic improvement in treated groups was consistent with haematological recovery, supporting the role of blood glucose control in the observed erythroprotective outcomes. The combined fruit and leaf extracts produced similarly favourable outcomes, while the leaf extract alone yielded limited benefit. These effects are mechanistically consistent with the potent antioxidant and anti-inflammatory phytochemical composition of the *K. africana* fruit. The dose of 1000 mg/kg employed was selected on the basis of prior literature and was not associated with overt toxicity during the study period; however, formal toxicity studies are required before clinical application. The findings provide scientific support for the traditional use of this plant in managing diabetes and its haematological complications. Future studies should conduct dose-response analyses, formally assess long-term safety, measure oxidative stress biomarkers and inflammatory cytokines, and employ a priori power calculations to determine adequate sample sizes.

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