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ANTIDIABETIC, ANTIOXIDANT AND HAEMATOPOIETIC POTENTIALS OF AQUEOUS, METHANOL AND PETROLEUM ETHER EXTRACTS OF UNRIPE *CARICA PAPAYA* SEED ON STREPTOZOTOCIN-INDUCED DIABETIC RATS

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ABSTRACT: *This study investigated the antioxidant and haematopoietic capacity of unripe Carica papaya (UCP) seed extract in diabetic rats using three different solvents. Thirty adult male Wistar rats were used but twenty-five rats were induced with diabetes following an overnight fast, by a single intravenous injection of 60 mg/kg STZ freshly dissolved in citrate buffer (pH 4.5). Control animals received 0.9% sterile saline. Hyperglycemia was confirmed for three (3) days. Rats with blood glucose levels ≥ 200 mg/dL were selected for the study. The rats were grouped into six groups of five rats per group: NC, normal control, DC, diabetic control, DAUCP, DMUCP, and DPEUCP are diabetic rats treated with aqueous, methanol petroleum ether extracts respectively while DSTD, diabetic rats treated with standard drug. The extracts were administered to the animals orally for 21 days. The animals administered with different extracts showed a significant decrease ($p<0.05$) in blood sugar level and Malondialdehyde (MDA) concentration but an increase in activities of superoxide dismutase (SOD), catalase (CAT) and concentration of reduced glutathione (GSH) when compared to the diabetic control group. Diabetic rats without treatment showed a significant decline in RBC count, WBCs and platelets and their associated indices except neutrophils in the diabetic rats without treatment. Treatment with the extracts significantly increases these haematological parameters. The extracts could improve glycemic control and improve haematological indices along with enhanced antioxidant enzyme activity which has a beneficial effect in preventing diabetic complications. This implies that unripe C. papaya seed could be used in the management of diabetes.*

KEYWORDS: Diabetes, *Carica papaya*, Oxidative stress, Hyperglycaemia and blood physiology.

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INTRODUCTION

Diabetes is a rapidly growing health challenge and potential epidemic across low- and middle-income countries like India and Nigeria (Ugwu *et al.,* 2011; Mathur *et al.,* 2022; Ugwu, 2023, Akukwu *et al.,* 2024, Omodara *et al.,* 2024). In the world, about five hundred and thirty-seven million (537,000,000) adults, (20-79 years) are living with diabetes making a ratio of 1 to 10 and this number is predicted to rise to 643 million by 2030 and 783 million by 2045 (IDF, 2021). In this estimated number, over 3 in 4 adults are living with diabetes in low- and middle-income countries and diabetes is responsible for 6.7 million deaths in 2021 (IDF, 2021). Diabetes mellitus can become more costly when complications of the disease occur and dialysis treatment also contributes to long-term burden and health budgets (Crasto, 2021, Kane *et al.,* 2021, Sharma *et al.,* 2022).

Hyperglycemia is one of the main reasons for reactive oxygen species (ROS) overproduction in diabetic conditions (Darenskaya *et al.,* 2021). Oxidative stress (OS) is a metabolic dysfunction mediated by the imbalance between the biochemical processes leading to elevated production of reactive oxygen species (ROS) and the antioxidant defence system of the body (Singh *et al.,* 2022; Akpoveso *et al.,* 2023, Maache *et al.,* 2024). In diabetes, excessive free radicals and reactive oxygen species (ROS) are generated through various pathways as a result of hyperglycemia. Sustained hyperglycaemia, as seen in diabetes, has been shown to induce cardiovascular complications through haematological alterations (Sampathkumar *et al.,* 2021). Assessment of haematological variables is a very common and primary diagnostic important routine for the clinical evaluation of the state of health (Yakubu *et al.,* 2007, Nwuke *et al.,* 2024). Examination of haematological variables helps to explain the blood-related functions of consumed substances (Arkew *et al.,* 2021).

Carica papaya (papaw or papaya) is one of the tropical and subtropical trees that is well known for having the entirety of its parts utilized. The properties of papaya fruit and other parts of the plant are also well known in traditional system of medicine (Sathyapalan *et al.,* 2020; Kamilla *et al.,* 2021; Ugwu, 2023, Ugwu *et al.,* 2023). Despite the availability of clinical therapeutic agents, patients may seek an option for alternative remedies (Sharma *et al.,* 2022), such as natural products, to control these complications and improve glycemic control and glucose intolerance (Furman *et al.,* 2020). Medicinal plants with hypoglycemic effects are used worldwide to treat diabetes with minimal side effects, a challenge for improving diabetes care (Rahman *et al.,* 2024). In this study, we investigated the antidiabetic, antioxidant and haematopoietic potentials of aqueous, methanol and petroleum ether extracts of unripe *Carica papaya* seed in streptozotocin-induced diabetic rats.

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MATERIALS AND METHODS

Chemicals/Reagents

All chemicals and reagents used in this research were of analytical grade. Streptozotocin (STZ) was purchased from Sigma Chemicals, (St. Louis, USA), others were obtained from Merck., while Kits for different enzyme assays were purchased from Biosystems S.A., Mexico.

Plant material

Unripe fruits of *Carica papaya* were harvested from a local farm at Okuku Yala Local Government Area of Cross River State, Nigeria. The plant was identified and authenticated by Dr Michael Eko, a botanist in the Department of Biological Sciences, University of Calabar and a voucher specimen number 73 was deposited in the Herbarium, Department of Botany, University of Calabar, Nigeria. The fruits were cut into pieces and the seeds were removed and thoroughly washed and dried at room temperature. Dried seeds were crushed and ground to powder using a domestic mixer grinder (binatone BLG-450).

Extraction using aqueous and organic solvents

The aqueous extraction was performed by soaking 400 g of powdered *C. papaya* seed in 1 L of distilled water over 48 hours. The extracts were filtered with Whatman filter paper no 1 (24 cm), dried at 40˚C and kept frozen at -20^{o}C for future use. It was reconstituted in distilled water for administration.

The methanol and petroleum ether extraction were performed each by wrapping a 400 g powder sample of *C. papaya* seeds in a thimble and placed in a 1000 cm^{3} Soxhlet extractor (M and G Scientific Co., England). The samples were Soxhlet extracted following standard analytical laboratory method at 60^{o}C for 72 h. The extracts were evaporated to dryness at 40˚C and kept frozen at -20^{o}C for use. It was reconstituted in Tween 80 for administration.

Animals

Thirty male Wistar rats weighing 130 to 160 g were used. The animals were maintained under laboratory conditions of temperature (23 to 25°C) and light 12 h light-dark cycle in the Animal House of the Department of Medical Biochemistry, Cross River University of Technology, Okuku Campus and allowed free access to grower's mash and water *ad libitum*. The animals were acclimatized for two weeks. The experiment which lasted for 21 days was carried out according to the guideline procedures of the Animal House. The rats were maintained in accordance with the principles of laboratory animal care guidelines (NIH, 2011). The experiment protocol was designed according to the Departmental Animal Ethics Committee guidelines.

Induction of Diabetes

Overnight-fasted rats were induced with diabetes by a single intraperitoneal injection of 60 mg/kg body weight of streptozotocin (STZ) freshly dissolved in citrate buffer (0.01 M, pH 4.5). Control animals received 0.9 % sterile saline. Hyperglycemia was confirmed 3 days after injection by measuring the tail vein blood glucose level with an Accu-Chek Active (Roche Diabetes Care GmbH, Mannheim, Germany). Animals with fasting blood glucose levels ≥ 200 mg/dL and ≤ 450 mg/dL were considered diabetic and used for the study.

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Experimental Design

Thirty male Wistar rats were used but the animals were divided into six groups, each group containing five animals (n=5).

NC: Normal Control

DC: Diabetic Control

DAUCP: Diabetic and 200 mg Aqueous Extract of unripe *C. papaya* seed

DMUCP: Diabetic and 200 mg Methanol Extract of unripe *C. papaya* seed

DPEUCP: Diabetic and 200 mg Petroleum Ether Extract of unripe *C. papaya* seed

DSTD: Diabetic and standard Drug (glibenclamide)

Duration of Treatment

Treatment began on the day the diabetic state was ascertained. Blood glucose level was determined weekly for three weeks throughout the period of the experiment.

Determination of Fasting Blood Glucose Level

Fasting blood glucose levels were determined by using a glucometer (Accu-chek Active) and test strips by glucose oxidase method. This was done weekly for three weeks.

Preparation of Tissue Homogenate

Organs (liver and kidneys) were excised, freed of surrounding tissues, blotted with clean tissue paper, weighed, and homogenized in ice phosphate buffer (0.1 M, pH 7.4), to obtain 10 % homogenate (w/v). The homogenates were centrifuged at 3000 rpm for 10 minutes to obtain the supernatants kept frozen overnight at –20◦C before being used in the assays.

Lipid Peroxidation and Antioxidant Determination

Malondialdehyde (MDA) was determined by using a method adapted from Khoschsorur *et al* (2000) The method of Rukkumani *et al.*· (2004) was followed in estimating the level of reduced glutathione (GSH). Superoxide dismutase (SOD) was determined by the method of Crosti *et al* (1987). Then catalase (CAT) activity was determined by the method of Aebi *et al* (1984).

Haematological Estimations

The blood samples were collected with a 5 mL syringe and needle by cardiac puncture, and transferred into clean EDTA and were immediately used for determination of haematological parameters. The haematology profile, which covers red blood cells (RBCs), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH)and mean cell haemoglobin concentration (MCHC), white blood cells (WBCs), lymphocytes (LYM), monocytes (MONO), basophils (BASO), and procalcitonin (PCT and neutrophils (NEUT), platelet count (PLT), mean platelet volume (MPV) and platelet distribution width count (PDWC), was determined using a Synchron CX5 autoanalyzer according to the manufacturer’s protocol.

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Statistical Analysis

The experimental data were analysed for statistical significance by one-way analysis of variance and post hoc comparison using the SPSS version 23. All data were reported as mean ± SD and statistical significance was accepted at $P< 0.05$.

RESULTS

Weekly Blood Glucose Level of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

Figure 1 shows the mean fasting blood glucose of experimental rats treated with the aqueous, methanol, petroleum ether extracts and glibenclamide. On day 0 there was a significant difference ($P<0.05$) between the normal control and other groups. Other groups except normal control exhibited hyperglycemia showing that induction of diabetics was successful. After the experimental period (3 weeks), STZ-diabetic rats exhibited significant ($P<0.05$) hyperglycemia compared with the control rats (Figure 1). The extracts and glibenclamide decreased blood glucose levels in the diabetic rats compared to the untreated diabetic rats ($P<0.05$). On day 7 the glucose level of the DC group increased when compared to day 0 while in the treated groups it reduced. On day 21 the reduction in glucose levels of DMUCP and DSTD was significant ($P<0.05$) when compared to DAUCP and DPEUCP. The reduction in glucose levels of DMUCP and DSTD were statistically similar. Among the extracts, DMUCP seems to be more potent in the reduction of glucose.

Oxidative Stress Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

In the diabetic control group, malondialdehyde (MDA) level was significantly ($P<0.05$) increased in the liver and kidney but glutathione (GSH) levels and activities of SOD and CAT were decreased significantly ($P<0.05$) in the liver in comparison to the normal control. MDA was significantly ($P<0.05$) decreased in the liver and kidney but GSH level and activities of SOD and CAT were increased significantly in the liver in all the treated groups when compared to the diabetic control.

Red Blood Cell (RBC) and RBC Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

A significant ($P<0.05$) decrease in the levels of red blood cells (RBCs), haemoglobin (HGB), haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH)and mean cell haemoglobin concentration (MCHC) in diabetic control groups were observed when compared with the normal control group. Treatment with extracts or glibenclamide exhibited a significant ($P<0.05$) increase in the levels of RBC, HGB, HCT, MCV, MCH and MCHC when compared to the diabetic control.

WBC Count and WBC Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

White blood cells (WBCs), lymphocytes (LYM), monocytes (MONO), basophils (BASO), and procalcitonin (PCT) showed a remarkable decrease in streptozotocin-induced diabetic control

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rats when compared to the normal control. Administration of the three extracts and glibenclamide significantly (P<0.05) restored the alterations in all these variables. But neutrophils (NEUT), exhibited a significant (P<0.05) increase in diabetic control rats when compared to the normal control. However, the treatment prevented further increases in the NEUT.

Platelet Count and Platelet Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

Platelet count (PLT), mean platelet volume (MPV) and platelet distribution width count (PDWC) showed a remarkable decrease in streptozotocin-induced diabetic control rats when compared to the normal control except in the MPV of DAUCP. MPV level was statistically similar in DC and DAUCP. Administration of the three extracts and glibenclamide significantly (P<0.05) restored the alterations in all these variables except in the MPV of DAUCP.

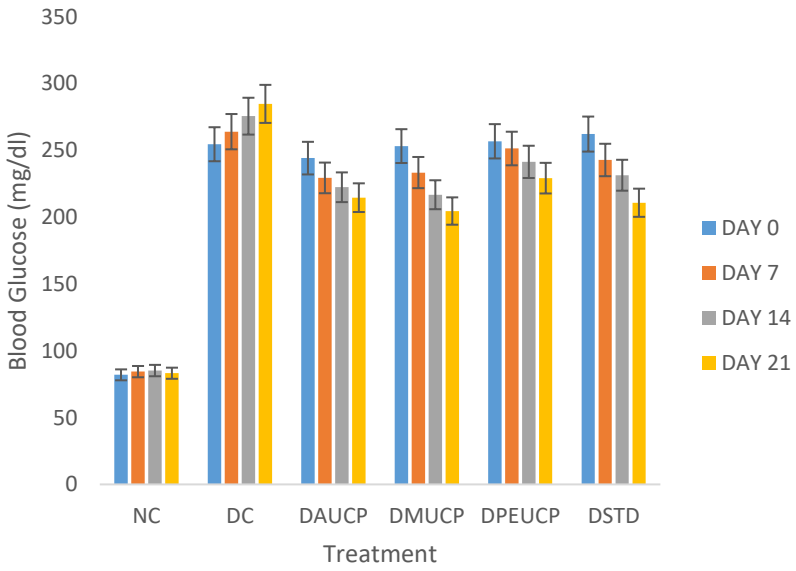

Figure 1: Weekly Blood Glucose Level of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide

Table 1: Liver Oxidative Stress Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

GROUP	SOD(U/min/mg of Protein)	CAT (U/min/mg of Protein)	MDA (µmol/mg of protein)	GSH (µmol/mg of protein)
NC	27.79±0.31^{d}	17.68±0.11^{e}	5.39±0.19^{a}	52.78±0.53^{f}
DC	15.49±0.27^{a}	8.71±0.15^{a}	11.72±0.33^{c}	32.11±0.84^{a}

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DAUCP	20.99±0.62^{c}	11.65±0.35^{c}	7.29±0.21^{b}	38.15±0.59^{c}
DMUCP	21.77±0.32^{c}	13.94±0.74^{d}	7.17±0.51^{b}	39.18±0.39^{d}
DPEUCP	19.36±0.68^{b}	10.85±0.44^{b}	7.16±0.26^{b}	36.65±0.51^{b}
DSTD	21.36±0.92^{c}	14.05±0.26^{d}	7.23±0.44^{b}	39.98±0.48^{e}

Values are means ±SD of five replicate determinations. Values with different superscript on the same row are statistically different (P<0.05).NC: Normal Control; DC: Diabetic Control; DAUCP: Diabetic + 200 mg Aqueous Extract of unripe *C. papaya* seed; DMUCP: Diabetic + 200 mg Methanol Extract of unripe *C. papaya* seed; DPEUCP: Diabetic + 200 mg Petroleum Ether Extract of unripe *C. papaya* seed; DSTD: Diabetic + 0.1 mg glibenclamide. SOD; superoxidase dismutase; CAT: catalase; GSH: glutathione.

Table 2: Kidney Oxidative Stress Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

GROUP	SOD (U/min/mg of Protein)	CAT (U/min/mg of Protein)	MDA (µmol/mg of protein)
NC	33.60±0.70^{e}	188.00±0.93^{e}	7.55±0.35^{a}
DC	16.42±0.45^{a}	50.82±0.37^{a}	13.94±0.29^{d}
DAUCP	26.40±0.35^{b}	98.48±2.32^{b}	8.95±0.76b^{c}
DMUCP	28.86±0.76^{d}	100.88±0.43^{cd}	8.83±0.52^{b}
DPEUCP	27.03±0.48^{b}	99.26±2.49^{bc}	8.56±0.36^{b}
DSTD	27.84±0.46^{c}	102.24±0.54^{d}	9.51±0.38^{c}

Values are means ±SD of five replicate determinations. Values with different superscript on the same row are statistically different (P<0.05).NC: Normal Control; DC: Diabetic Control; DAUCP: Diabetic + 200 mg Aqueous Extract of unripe *C. papaya* seed; DMUCP: Diabetic + 200 mg Methanol Extract of unripe *C. papaya* seed; DPEUCP: Diabetic + 200 mg Petroleum Ether Extract of unripe *C. papaya* seed; DSTD: Diabetic + 0.1 mg glibenclamide. SOD; superoxidase dismutase; CAT: catalase; GSH: glutathione.

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Table 3: RBC and RBC Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

GROUP	RBC ($x10^{12}$/L)	HB (g/dL)	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g/dL)	RDWC (%)
NC	8.19 ± 0.26^{c}	15.37 ± 0.19^{c}	52.86 ± 0.29^{d}	68.29 ± 0.29^{d}	19.29 ± 0.33^{c}	32.99 ± 0.28^{c}	16.43 ± 0.21^{a}
DC	6.43 ± 0.05^{a}	10.06 ± 0.30^{a}	35.62 ± 0.50^{a}	56.13 ± 0.20^{a}	15.19 ± 0.16^{a}	28.33 ± 0.45^{a}	18.06 ± 4.23^{a}
DAUCP	7.68 ± 0.11^{b}	14.51 ± 0.32^{b}	50.56 ± 0.41^{b}	69.30 ± 0.72^{e}	20.43 ± 0.38^{d}	31.33 ± 0.38^{b}	16.56 ± 0.25^{a}
DMUCP	8.10 ± 0.19^{cd}	15.10 ± 0.31^{c}	51.44 ± 0.34^{bc}	67.36 ± 0.44^{c}	20.30 ± 0.63^{d}	33.90 ± 0.97^{d}	16.54 ± 0.30^{a}
DPEUCP	7.83 ± 0.31^{bc}	14.98 ± 0.40^{c}	51.64 ± 1.35^{c}	66.36 ± 0.20^{b}	18.59 ± 0.35^{b}	32.38 ± 0.73^{c}	16.68 ± 0.47^{a}
DSTD	8.30 ± 0.29^{c}	15.14 ± 0.38^{c}	52.04 ± 0.61^{cd}	67.99 ± 0.51^{d}	19.20 ± 0.26^{c}	32.72 ± 0.66^{c}	18.52 ± 4.41^{a}

Values are means ± SD of five replicate determinations. Values with different superscripts on the same row are statistically different ($P<0.05$). NC: Normal Control; DC: Diabetic Control; DAUCP: Diabetic + 200 mg Aqueous Extract of unripe *C. papaya* seed; DMUCP: Diabetic + 200 mg Methanol Extract of unripe *C. papaya* seed; DPEUCP: Diabetic + 200 mg Petroleum Ether Extract of unripe *C. papaya* seed; DSTD: Diabetic + 0.1 mg glibenclamide. RBC: Red Blood Cell; HB: Haemoglobin; HCT: Haematocrit; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Haemoglobin; MCHC: Mean Corpuscular Haemoglobin Concentration; RDWC: Red Cell Distribution Width

Table 4: WBC Count and WBC Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

GROUP	WBC ($x\ 10^{9}$/L)	LYM (%)	MONO (%)	EOSINO (%)	BASO (%)	NEUT (%)	PCT (%)
NC	9.17 ± 0.46^{b}	52.04 ± 0.68^{d}	5.23 ± 0.09^{b}	4.02 ± 0.07^{b}	1.66 ± 0.11^{e}	42.56 ± 0.31^{c}	0.46 ± 0.02^{c}
DC	5.59 ± 0.30^{a}	40.94 ± 0.74^{a}	3.36 ± 0.42^{a}	2.30 ± 0.18^{a}	0.80 ± 0.07^{a}	50.98 ± 0.47^{d}	0.42 ± 0.01^{a}
DAUCP	9.15 ± 0.30^{b}	48.87 ± 0.48^{c}	4.91 ± 0.37^{b}	4.08 ± 0.08^{b}	1.04 ± 0.19^{b}	38.90 ± 0.34^{a}	0.47 ± 0.02^{c}
DMUCP	9.29 ± 0.12^{b}	49.16 ± 0.30^{c}	5.01 ± 0.14^{b}	4.12 ± 0.13^{b}	1.27 ± 0.05^{c}	40.19 ± 0.77^{b}	0.44 ± 0.02^{ab}
DPEUCP	9.36 ± 0.05^{b}	46.49 ± 0.47^{b}	5.12 ± 0.22^{b}	4.22 ± 0.30^{b}	1.43 ± 0.05^{d}	39.01 ± 0.40^{a}	0.45 ± 0.03^{c}
DSTD	9.46 ± 0.06^{b}	48.80 ± 0.48^{c}	5.16 ± 0.45^{b}	4.03 ± 0.18^{b}	1.47 ± 0.05^{d}	39.32 ± 0.59^{a}	0.44 ± 0.02^{ab}

Values are means ± SD of five replicate determinations. Values with different superscripts on the same row are statistically different ($P<0.05$).NC: Normal Control; DC: Diabetic Control; DAUCP: Diabetic + 200 mg Aqueous Extract of unripe *C. papaya* seed; DMUCP: Diabetic + 200 mg Methanol Extract of unripe *C. papaya* seed; DPEUCP: Diabetic + 200 mg Petroleum Ether Extract of unripe *C. papaya* seed; DSTD: Diabetic + 0.1 mg glibenclamide. WBC: white blood count; LYM: lymphocytes; MONO: monocytes; EOSINO: eosinophil; BASO: basophil; NEUT: neutrophils; PCT: Procalcitonin

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Table 5: Platelet Count and Platelet Indices of Rats treated with Aqueous, Methanol, Petroleum Ether extracts and Glibenclamide.

GROUP	PLT (x 10^9/L)	MPV (fl)	PDWC (fl)
NC	510.20±0.99^e	8.10±0.28^b	17.35±0.49^c
DC	408.94±1.08^a	6.50±0.35^a	10.64±0.58^a
DAUCP	492.60±3.52^c	6.27±0.28^a	15.42±0.47^b
DMUCP	497.90±3.56^d	7.90±0.39^b	17.38±0.45^c
DPEUCP	487.36±4.54^b	8.13±0.29^b	15.61±0.53^b
DSTD	499.17±4.69^d	7.68±0.33^b	17.22±0.34^c

Values are means ± SD of five replicate determinations. Values with different superscripts on the same row are statistically different (P<0.05).NC: Normal Control; DC: Diabetic Control; DAUCP: Diabetic + 200 mg Aqueous Extract of unripe *C. papaya* seed; DMUCP: Diabetic + 200 mg Methanol Extract of unripe *C. papaya* seed; DPEUCP: Diabetic + 200 mg Petroleum Ether Extract of unripe *C. papaya* seed; DSTD: Diabetic + 0.1 mg glibenclamide. PLT: platelets; MPV: mean platelets volume; PDWC: platelets distribution width count.

DISCUSSION

Oxidative stress describes a physiological state in which the formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) attains disproportionate levels, either by excess production or reduced removal due to the overwhelming antioxidant capacity of the system (Forcados *et al.,* 2017; Unuofin and Lebel, 2020). According to Tsai *et al* (1994) and Kawamura *et al* (1994) elevated blood sugar levels enhance the production of ROS during lipid degradation of low-density lipoprotein (LDL). In this study, there was a significant increase in MDA and a decline in SOD, CAT and GSH in both the liver and kidney tissues of the diabetic control groups. Several reports have shown that there is a close association between oxidative stress and DM due to increased oxidative damage to vital macromolecules (Bhattacharya *et al.,* 2018, Malekiyan *et al.,* 2019, Akpoveso *et al.,* 2023). The increase in MDA and reduction in the activities of SOD and CAT and reduction in the concentration of GSH observed in this study was in line with other previous studies which indicated that these parameters were altered in diabetic rats (Ugwu *et al.,* 2013; Asuk *et al.,* 2015). The treatments significantly ameliorated these alterations which indicates that the extracts possess antioxidant potentials which have helped in scavenging the free radicals.

Hyperglycaemia which causes increased formation of ROS has been shown to impair RBC deformability, further causing an increase in RBC haemolysis (Wilkins *et al.,* 2002; Abbas *et al.,* 2017). The impairment in RBC deformability is correlated with haematological changes which include reduced RBC count, Hb concentration, HCT levels, MCV, MCHC, and RDW concentration as demonstrated by the hyperglycaemic STZ-induced diabetic animals in this study (Lippi *et al.,* 2014; Gamede *et al.,* 2018). The three extracts, however, significantly improved the haematological parameters. The ability of the extracts to significantly improve the haematological parameters may be due to the extracts' ability to decrease blood glucose and improve antioxidant status since this study has shown the ability of extracts to improve

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SOD, CAT and GSH in STZ-induced diabetic rats. This might signify its protective action by counteracting diabetes-induced stress, hence attenuating the oxidative stress induced β-cell damages and also protecting them against functional overstrain (Reiter *et al.,* 2009; Hajam *et al.,* 2018, Krishnamurti *et al.,* 2022).

In diabetic rats total WBC count and its associated indices showed a remarkable decrease, which is supported by previous studies that total white blood cell count (WBCC) and lymphocyte count decreases (Hillson, 2015) in diabetic conditions. The decrease in WBC and lymphocytes could be interrelated tothe inhibition of leukocytes from the bone marrow which might be due to the poor defensive mechanism against infection (Oyedemi *et al.,* 2011). Diabetic rats were given the extracts for three weeks significantly restored the WBC count and lymphocytes. Polymorphs which include neutrophils, eosinophils and basophils are involved in different immune defence processes (Ani *et al.,* 2022). Therefore, diabetic patients are susceptible to any kind of infection, which results in high morbidity and mortality. Thus an increase in WBC and lymphocyte counts improves the immune status of diabetic rats and makes them more resilient against opportunistic infections.

In the present study diabetes rats showed an increment in platelet count. Earlier studies are in support, which reported that diabetes causes multiple abnormalities such as platelet hyper-reactivity with higher adhesiveness, activation and aggregation (Hillson, 2015). The platelet abnormalities are related to increased clotting, impaired clot breakdown, endothelial dysfunction, and platelet hyper-reactivity. All these factors amplify the threat of atherothrombotic incidents in diabetes (Hillson, 2015). The administration of the extracts significantly revised the platelet count towards the normal control and might prevent their hyper-reactivity.

CONCLUSION

The alterations observed in the study were revised following the administration of the extracts. It shows that the extracts have antidiabetic, antioxidant and haematopoietic potentials which help in the management of diabetes.

AUTHORS' CONTRIBUTIONS

UMN, OHA and EEO conceived and designed the study. BCO, OCI, EIG and PUV performed the experimental aspect of the study. UMN, OHA and OCI wrote the manuscript. UMN, OCG and BCO analyzed and interpreted the statistical analysis, and EEO and OCG contributed to the editing and proofreading of the manuscript. All the authors consent to be accountable for every aspect of the paper.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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