FEDERAL UNIVERSITY OF TECHNOLOGY,

MINNA, NIGER STATE, NIGERIA

SCHOOL OF LIFE SCIENCES

INTERNATIONAL CONFERENCE

BOOK OF PROCEEDING

Theme:

WEALTH CREATION FROM TRANSLATIONAL RESEARCH

MON. 5TH - THUR. 8TH AUGUST, 2024.

Vol. 1: 186 – 193 (2024)

ffect of Methanol Extract of *Calotropis procera* Flower on Blood Glucose and Selected iochemical parameters in Alloxan-Induced Diabetic Rats

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ABSTRACT

Diabetes remains a major burden on global health and is one of the most common causes of death worldwide. This study determined the effect of methanol extract of *Calotropis procera* flower (MECPF) on glucose level and some biochemical parameter on alloxan-induced diabetic rats. Thirty Wistar rats were divided into six groups of five animals each; normal, diabetic non-treated, 100, 200 and 400 mg/kgbw of extract and standard drug groups. At the end of the experiment the rats were euthanized and the blood samples were collected for glucose, kidney, liver biomarkers and lipid profile were analysed using standard procedures (or using automated blood Analyzer). A significant elevation of glucose level (250 mg/dl), creatinine, urea and uric acid were observed in diabetic non-treated group compared to *Calotropis procera* groups. There was also significant ($p \leq 0.05$) increase in cholesterol (470.01 mg/dl), triglyceride (196.74 mg/dl), LDL-C (69.06), ALT (91.57 U/L), AST (78.30 U/L), ALP (139.83 U/L), bilirubin (0.94 mg/dl) with decrease in total protein (12.49 g/dl), albumin (8.77mg/dl) and HDL-C (57.76 mg/dl) in diabetic non-treated when compared with those treated with MECPF. Administration of MECPF were able to significantly ($p \leq 0.05$) reversed the levels of glucose, kidney, liver biomarkers and lipid abnormalities. Hence, methanol extract of *Calotropis procera* flower could be explored further to obtain the active compound for the management of diabetes. The result section of the abstract should show how effective the plant extract is by comparing with the standard drug

Keywords: *Calotropis procera*, Diabetes, methanol, glucose, biochemical parameters

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INTRODUCTION

Diabetes is a chronic disorder in the metabolism of carbohydrates, proteins, and fat due to absolute or relative deficiency of insulin secretion with/without varying the degree of insulin resistance (Egbuna *et al*., 2021). Effective blood glucose control is the key to preventing or reversing diabetic complications and improving the quality of life in patients with diabetes (Garg and Duggal, 2022). Diabetes also gives rise to various secondary problems such as cataracts, microvascular problems, and neuropathy (Ansari *et al*., 2022). Similarly, a major cause of death worldwide and a significant burden on global health is

diabetes (Davies *et al.*, 2023). The International Diabetes Federation (IDF) estimates that 451 million individuals in the world between the ages of 18 and 99 have diabetes, and 693 million are predicted to have the disease by 2045 (Davies *et al.*, 2023). Regrettably, management of diabetes without side effects is still challenging to the medical community. However, pharmacological and clinical trials of medicinal plants have shown anti-diabetic effects with little or no side effects (Yedjou *et al.*, 2023).

The leaves of *Calotropis procera* plant have been mostly used as antidiabetic agent among local populace in Nigeria in various form. As such myriads of scientific reports are available to buttress such claim. Nevertheless, despite the uses of *C. procera* flower concoction to manage the same diabetes among the local populace in Nigeria, there are scarce scientific back-up to these effects. Although, from our previous study, phytochemical constituents and effect of methanol extract of *Calotropis procera* flower on haematological parameters in alloxan-induced diabetes in Wistar rats were reported (Hamzah *et al.*, 2024). However, effects of the methanol extract of *Calotropis procera* flower n kidney and liver function indices in alloxan-induced diabetes in Wistar have not been established. Therefore, it is worthwhile to investigate the effect of methanol extract of *calotropis procera* flower on blood glucose and selected biochemical parameters in alloxan-induced diabetic rats.

MATERIALS AND METHODS

Collection and Identifications of the Plant Materials

The fresh stalks of *Calotropis procera* carrying the flowers were collected within the premises of Federal University of Technology Minna, Niger State, Nigeria, Bosso Local Government Area on October 2023. The plant was authenticated in the Botany Department, Federal University of Technology Minna, Niger State by Dr. Daudu O.A.Y. The voucher number FUT/PLB/ASC/004 was allotted to the plant and the specimen was deposited at the herbarium of Botany Department, Federal University of Technology Minna, Niger State.

Figure 1: *Calotropis procera* Flower

Preparation of Plant Sample

Fresh *Calotropis procera* flowers were removed from the stalks, washed with distilled water and then air dried at room temperature (28°C) for three weeks. Afterwards, the dried flowers were pulverized using a rotary blender. The powdered flower was kept in a plastic tight container till further use.

Extraction of *C. procera* Flower

Two hundred and fifty grams (250 g) of pulverized *C. procera* flower was macerated with 1,500 mL of absolute

methanol. The mixture was occasional shaken for 72 hours. Afterwards, the extract was filtered with filter paper after which the methanol was evaporated at 50°C under reduced pressure in a rotary vacuum evaporator. The molten form of the methanol extract was later completely dried in water bath at 50°C

Experimental Animals

Wistar albino rats of weight (79g – 174g) were used for experiment and were obtained from Animal House of the Department of Biochemistry, School of Life Sciences, Federal University of Technology, Minna. The Wistar rats were allowed to acclimatize afterward for one week. The ethical clearance was obtained on the 15th of January, 2024 from the Ethical Committee of Federal University of Technology Minna, Niger State Nigeria with ethical number 000057.

Induction of Diabetes

The rats were placed on overnight fasting with but was allowed access to water. Exactly 180 mg/kg bodyweight of alloxan monohydrate was administered intraperitonially to rats in the respective groups except the normalglyceamic group which was given alloxan equivalent volume of cold physiological saline. Fasting blood glucose was checked after 72 hours and rats with blood glucose ≥ 150 mg/dl were considered diabetic and selected for the study. The treatment went on daily for seven days and the animal euthanized on the 7th day.

Animal Grouping and Treatment of Animals

The animal grouping and their respective treatment is shown below:

Group 1: Non-diabetic + 0.2 mL of distilled water

Group 2: Diabetic + 500 µg/kg bw. of Glibenclimide

Group 3: Diabetic + 0.2 ml. of distilled water

Group 4: 100 mg/kg bw. of methanol extract of *C. procera* flower

Group 5: 200 mg/kg bw. of methanol extract of *C. procera* flower

Group 6: 400 mg/kg bw. of methanol extract of *C. procera* flower

Determination of Glucose Concentration

The levels of glucose in the blood of each and every experimental rat were monitored on a regular basis during the course of the experiment. Following the collection of blood samples from the tip of the animal's tail, an Accu-Check glucometer was utilized in order to determine the blood glucose levels of the animal (Roche Diagnostics, USA).

Collection of Blood Sample

At the end of this treatment, rats were anesthetized under low concentrated chloroform vapor and euthanized after 7th day and the blood samples were collected via cervical dislocation for some biochemical parameters analysis.

Determination of Kidney, Liver Function Indices and Lipid Profile

Kidney function indices including urea, creatinine and uric concentrations were determined using Randox kits (Randox Laboratories Limited, United Kingdom) following the manual instructions

Liver function Indices such as Alanine Aminotransferase (ALT), Aspartate

Aminotransferase (AST), Alkaline Phosphatase (ALP), Albumin and Bilirubin concentration were determined using commercial kit (AGAPE, Switzerland) and the direct biuret method were used to estimate the total protein level. Lipid Profiles of the blood samples were also estimated using commercial kit (which of the kits)

Data Analysis

The collected data was analyzed using SPSS software package. Analysis of variance (ANOVA) was used to evaluate the outcomes, which were presented as the mean value ± standard error of the mean. This was followed by performing Duncan's Multiple Range Test at a confidence level of $p < 0.05$.

RESULTS

Effect of Methanol Extract of *Calotropis procera* Flower on Blood Glucose levels in Alloxan-induced Diabetes in Wistar Rats

Administration of alloxan monohydrate to the experimental rats significantly increased the level of blood glucose in the proportion of 2.47, 2.21 and 1.16 at their respective D0, D3 and D7 respectively when compared with non-diabetic rats that were administered with distilled water. However, administration of 100, 200 and 400 mg/kg body weight (bw.) of methanol extract of *Calotropis procera* flower (MECPF) significantly ($p \leq 0.05$) decreased the blood glucose level n D7 at 60.46%, 64.04% and 65.07% respectively at doses 100 mg/kg bw., 200 mg/kg bw., 400 mg/kg bw. when compared with diabetic rats that were treated with distilled water. Also, no significant ($p \geq 0.05$) difference between the blood glucose levels of all the doses of MECPF treated rats.

Table 1: Effect of Methanol Extract of *Calotropis procera* Flower on Blood Glucose levels in Alloxan-induced Diabetes in Wistar Rats

GROUP	DAY 0 (D0)	Day 3 (D3)	Day 7 (D7)
Group 1	117.00 ± 11.73^a	105.00 ± 6.00^a	89.67 ± 5.51^a
Group 2	406.33 ± 18.35^c	338.33 ± 32.89^d	292.00 ± 5.00^c
Group 3	313.67 ± 19.50^b	142.33 ± 28.30^b	65.67 ± 10.60^a
Group 4	294.33 ± 13.23^d	198.67 ± 21.07^c	115.33 ± 14.21^b
Group 5	260.67 ± 138.29^c	195.33 ± 33.71^c	105.00 ± 12.50^b
Group 6	222.67 ± 95.87^b	187.67 ± 29.15^c	102.00 ± 15.29^b

The values are expressed as the mean ± the standard deviation (SD). There is significant difference ($p < 0.05$) between values in the same column that have the different alphabet superscript.

Group 1: Non-diabetic + 0.2 ml. of distilled water, Group 2: Diabetic + 500 µg/kg bw. of Glibenclimide, Group 3: Diabetic + 0.2 mL of distilled water, Group 4: 100 mg/kg bw. of methanol extract of *C. procera* flower, Group 5: 200 mg/kg bw. of methanol extract of *C. procera* flower, Group 6: 400 mg/kg bw. of methanol extract of *C. procera* flower

Effect of Methanol Extract of *C. procera* Flower on Liver Function Indices in Alloxan-induced Diabetes in Wistar Rats

alloxan monohydrate to the Wistar rats significantly ($p \leq 0.05$) increased the levels of serum ALT, AST, ALP and bilirubin in the proportion of 0.56, 0.59, 0.35 and 1.04 while the total protein and albumin significantly ($p \leq 0.05$) decrease respectively when compared with non-diabetic rats that were administered with distilled water. However, administration of 100, 200 and 400 mg/kg body weight (bw.) of MECPF significantly ($p \leq 0.05$) decreased the activities/levels of serum ALT, AST, ALP and bilirubin in the proportion and significantly ($p \leq 0.05$) decreased the total protein and albumin when compared with diabetic rats that were treated with distilled water. Also, no significant ($p \geq 0.05$) difference between the activities/levels of serum ALT, AST, ALP, total protein, albumin and bilirubin of 100, 200 and 400 mg/kg body weight (bw.) of MECPF treated rats.

Table 2: Effect of Methanol Extract of *C. procera* Flower on Liver Function Indices in Alloxan-Induced Diabetes in Wistar rats

GROUP	ALT (U/L)	AST (U/L)	ALP (U/L)	Total Protein (g/dl)	Albumin (mg/dl)	Bilirubin (mg/dl)
Group 1	58.50±2.18^{b}	49.21±1.55^{cd}	103.99±2.24^{a}	24.91±0.95^{a}	16.29±1.78^{cd}	0.46±0.03^{a}
Group 2	91.57±1.71^{a}	76.30±3.44^{a}	139.83±2.61^{a}	12.49±0.64^{e}	8.77±0.43^{e}	0.94±0.30^{ab}
Group 3	57.33±1.41^{b}	57.41±1.76^{b}	127.38±1.88^{b}	19.41±1.40^{b}	12.79±0.76^{b}	0.62±0.56^{c}
Group 4	57.17±2.16^{b}	51.11±2.01^{bc}	120.79±2.34^{b}	19.95±1.82^{b}	14.15±1.54^{bc}	0.56±0.40^{bc}
Group 5	53.32±1.98^{bc}	49.53±2.36^{cd}	107.67±2.33^{a}	24.85±1.46^{a}	15.31±0.77^{b}	8.51±0.02^{a}
Group 6	44.76±2.44^{c}	42.50±6.30^{d}	101.68±2.46^{a}	20.82±1.39^{bc}	12.90±0.92^{bcd}	0.39±0.02^{cd}

The values are expressed as the mean ± the standard deviation (SD). There is significant difference ($p < 0.05$) between values in the same column that have the different alphabet superscript.

Group 1: Non-diabetic + 0.2 mL of distilled water, Group 2: Diabetic + 500 µg/kg bw. of Glibenclimide, Group 3: Diabetic + 0.2 mL of distilled water, Group 4: 100 mg/kg bw. of methanol extract of *C. procera* flower, Group 5: 200 mg/kg bw. of methanol extract of *C. procera* flower, Group 6: 400 mg/kg bw. of methanol extract of *C. procera* flower

Effect of Methanol Extract of *C. procera* flower on Lipid Profile of Alloxan-Induced Diabetes in Wistar rats

Administration of alloxan monohydrate to the experimental rats significantly ($p \leq 0.05$) increased the concentrations of serum cholesterol (Chol.), triglyceride (Trig.) and low-density lipoprotein cholesterol (LDL-C) with significant decreased in high-density lipoprotein in the proportion of 3.35, 1.15, 0.53 and 0.51 respectively when compared with non-diabetic rats that were administered with distilled water. However, administration of 100, 200 and 400 mg/kg body weight (bw.) of MECPF significantly ($p \leq 0.05$) decreased the reverted the mentioned lipid parameters when compared with diabetic rats that were treated with distilled water.

Table 4: Effect of Methanol Extract of *C. procera* flower on Lipid Profile of Alloxan-Induced Diabetes in Wistar rats

GROUP	Cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
Group 1	108.21 ± 2.50	92.38 ± 3.87	129.00 ± 2.23	65.86 ± 2.14
Group 2	470.31 ± [illegible]	196.74 ± 1.95	52.76 ± 1.52	166.90 ± 2.23
Group 3	150.21 ± 2.90	276.59 ± 2.51	118.35 ± 2.56	334.123 ± 1.10
Group 4	205.56 ± 4.22	128.88 ± 3.74	116.66 ± 2.27	127.35 ± 1.42
Group 5	255.72 ± 3.25	110.74 ± 2.72	125.46 ± 1.57	111.45 ± 2.24
Group 6	255.17 ± 2.59	50.76 ± 4.65	126.13 ± 2.81	117.97 ± 3.12

The values are expressed as the mean ± the standard deviation (SD). [illegible] values in the same column that share the different [illegible] superscripts.

Group 1: Non-diabetic + 0.2 mL of distilled water, Group 2: Diabetic + 500 µg/kg bw. of Glibenclimide, Group 3: Diabetic + 0.2 mL of distilled water, Group 4: 100 mg/kg bw. of methanol extract of *C. procera* flower, Group 5: 200 mg/kg bw. of methanol extract of *C. procera* flower, Group 6: 400 mg/kg bw. of methanol extract of *C. procera* flower.

Effect of Methanol Extract of *Calotropis Procera* Flower on Kidney Function Indices in Alloxan-induced Diabetes in Wistar Rats

Administration of alloxan monohydrate to the experimental rats significantly ($p < 0.05$) increased the concentrations creatinine (26.51 ± 1.25 µmol/L), urea (57.35 ± 2.37 µmol/L), uric acid (25.07 ± 2.92 µmol/L), sodium (270.46 ± 3.23 mEq/L), potassium (15.05 ± 0.16 mEq/L) and bicarbonate (39.26 ± 0.51 mEq/L). Nevertheless, administration of 100, 200 and 400 mg/kg body weight (bw.) of MECPF significantly ($p \leq 0.05$) decreased the levels of creatinine, urea, uric acid, sodium ion, potassium ion and bicarbonate ion when compared with diabetic rats that were treated with distilled water.

Table 5: Effect of Methanol Extract of *Calotropis Procera* Flower on Kidney Function Indices in Alloxan-induced Diabetes in Wistar Rats

GROUP	Creatinine (µmol/L)	Urea (µmol/L)	Uric acid (µmol/L)	Sodium (mEq/L)	Potassium (mEq/L)	Bicarbonate (mEq/L)
Group 1	10.06 ± 0.55	23.27 ± 1.01	10.07 ± 5.23	154.74 ± 3.13	7.47 ± 3.59	20.56 ± 0.99
Group 2	26.51 ± 1.25	57.35 ± 2.37	25.07 ± 2.92	270.46 ± 3.23	15.05 ± 0.16	39.26 ± 0.51
Group 3	14.22 ± 0.26	34.93 ± 15.25	28.10 ± 0.68	152.11 ± 2.35	11.72 ± 0.64	24.51 ± 2.27

Group 4	1.[illegible]8 ± [illegible]	24.44 ± 1.30[illegible]	15.1[illegible] ± [illegible]	153.3[illegible] ± 3.3[illegible]	11.7[illegible] ± 2.7[illegible]	32.4[illegible] ± 4.2[illegible]
Group 5	[illegible] ± [illegible]	23.24 ± 1.3[illegible]	14.24 ± [illegible]	157.[illegible] ± [illegible]	[illegible] ± [illegible]	14.27 ± 3.3[illegible]
Group 6	3.33 ± 1.12[illegible]	24.66 ± 1.4[illegible]	9.77 ± 0.26[illegible]	153.33 ± 2.1[illegible]	15.79 ± 6.8[illegible]	24.26 ± 1.2[illegible]

The values are expressed as the mean ± the standard deviation (SD). [illegible] significant differences [illegible] ($p < 0.05$) differences ($p < 0.05$) between values in the same column that have [illegible]

Group 1: Non-diabetic + 0.2 mL of distilled water, Group 2: Diabetic + 500 µg/kg bw. of Glibenclamide, Group 3: Diabetic + 0.2 mL of distilled water, Group 4: 100 mg/kg bw. of methanol extract of *C. procera* flower, Group 5: 200 mg/kg bw. of methanol.

DISCUSSIONS

Potency of an antidiabetic agent is connected to the hypoglycaemic activities of such agent. In this study MECPF extract was able to bring down the sugar level at D7 to denote its antidiabetic potential. Although there are scarce report to show the antidiabetic potential of flower extract of *C. procera*, however, antidiabetic potential of *Calotropis gigantea* white flower extracts have been established in alloxan-induced diabetic rats (Manivannan and Shopna, 2017). Liver is the largest organ in the body and it is known to be responsible for synthesis, metabolism, biotransformation, excretion of several xenobiotics (Pant et al., 2023). Significant increase of liver damage biomarkers was connected to the alloxan-induced toxicity. Report confirmed it that the leakages of the liver function enzymes into the blood stream could be connected to hepatic cells membrane destruction (Muhammad *et al*., 2018). Therefore, the reversion of these enzymes after MECPF extract might be as a result of antioxidant activities of the extract due to the presence of quercetin, caffeic acid, kaempferol, isorhamnetin as revealed by our previous study (Hamzat *et al*., 2024). Quercetin, caffeic acid, kaempferol and isorhamnetin are phenolic compounds that could have scavenged the reactive oxygen species (ROS) induced by the activity of alloxan. Hyperlipidemia is one of the complications that is associated with diabetes mellitus (Busari *et al*., 2015). The hypolipidemic effects displayed by MECPF treated diabetic animals could be as a result the phenolic constituent as well. This finding is similar to that of Manivannan and Shopna (2017) who also reported antihyperlipidemic of *Calotropis gigantea* white flower extracts in alloxan induced diabetic rats. Antidiabetic activity of *Calotropis gigantea* white flower extracts in alloxan induced diabetic rats. The activation of hepatocyte LDL receptors, which are in charge of absorbing LDL into the liver and subsequently lowering blood LDL levels, might have resulted from the control of cholesterol synthesis (Luciani *et al*., 2024). In a similar vein, MECPF reductions in lipids have been associated with increases in insulin levels (Busari *et al*., 2015). Furthermore, electrolyte imbalance is associated with diabetes as also shown in elevation in kidney damaged markers displayed this study (A. Shehri *et al*., 2021). Therefore, the alteration in the electrolytes of MECPF treated diabetic rats could be connected to the ameliorative effects of the MECPF in the kidney tissue since diabetes is also associated with nephropathy. The improvement in the kidney tissue could also be observed via

(2026). Wim reported that *A. indica* extracts, particularly azadirachtin and quercetin, interfered with seed germination and nutrient absorption by target plants. This suggests that the application of *A. indica* extracts can have dual effects: while they suppress weed growth, they may also negatively affect the germination and vigour of crops like maize as shown in this study. Hence, these findings are consistent with earlier research that has demonstrated both the potential and challenges of using *A. indica* extracts in agriculture. Agarwal *et al* (2021) also reported that aqueous application of *A. indica*-based extracts can inhibit seedling growth in rice and mustard which support the inhibitory effects observed in this study on maize seedlings. The inhibition observed across all concentrations suggests that maize may be particularly sensitive to allelochemicals present in *A. indica*, which requires careful management in agricultural systems.

The findings related to the seedling vigour index further reinforce the inhibitory nature of *A. indica* extracts. The significant reduction in vigour at higher concentrations indicates that maize growth could be substantially hampered in fields treated with high doses of *A. indica*-based products. This aligns with Farooq *et al* (2021), who emphasized that while *A. indica* can be beneficial for weed control and pest management, its phytotoxic effects must be mitigated to avoid unintended consequences on crop yield.

Therefore, in terms of practical applications, the results of this study suggest that while *A. indica* based products offer promising alternatives to synthetic pesticides and herbicides, their use in maize farming should be approached with caution. As the allelopathic effects on maize germination and growth highlight the need for controlled application to avoid detrimental impacts on crop performance. Finally, as suggested by Singh *et al* (2022), the integration of this type pesticidal plant in sustainable farming practices should focus on optimizing concentration levels and application methods to balance its benefits and risks.

CONCLUSION

The ethyl acetate and N-hexane extracts of *A. indica* at lower concentrations have weak allelopathic effects on the germination and early growth stages of maize. The use of lower concentration of the plant extracts should be considered for pesticides or herbicides during maize production so as to avoid poor growth, plant death and other unintended consequences during crop productivity.

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restoration of other kidney damage markers in MECPF treated diabetic rats.

In conclusion, oral administration of MECPF to alloxan induced-diabetes in rats corrected hyperglycaemia, hyperlipidemia, electrolyte imbalance, liver and kidney function markers associated with diabetes complications.

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