



Determination of Potential Anti-Diabetic Phytochemicals in Locally Grown *Gongronema latifolium* Leaf Extract Against Therapeutic Targets of Type-2 Diabetes Mellitus in Alloxin Induced Hyperglycemic Rats

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Received: June 19, 2025; Accepted: August 14, 2025; Published: August 24, 2025.

Doi: <https://doi.org/10.5281/zenodo.16937607>

Abstract: Type-2 diabetes mellitus is a metabolic disorder characterized by insulin deficiency, often leading to severe complications. This study investigated the anti-diabetic potential of *Gongronema latifolium* leaf extract against therapeutic targets of type-2 diabetes in alloxan-induced hyperglycemic rats. Diabetes was induced by intraperitoneal injection of alloxan monohydrate (150 mg/kg), after which six diabetic groups were treated with ethanol extracts of *G. latifolium* leaves at concentrations of 12.5, 25, 50, 100, and 125 mg/kg body weight. Control and diabetic control groups were also included. Key biochemical parameters fasting blood glucose, glycated hemoglobin (HbA1c), serum urea, creatinine, electrolytes, glutathione-S-transferase (GST), superoxide dismutase (SOD), malondialdehyde (MDA), and phytochemical profiles were analyzed using standard biochemical methods and automated chemistry analyzer (Smart Chem 200). Results revealed significant reductions ($p < 0.05$) in fasting blood glucose across all treatment groups, with mean values ranging between 32–93 mg/dl, compared to 182–256 mg/dl in untreated diabetic rats. Similarly, HbA1c levels significantly declined (16–40 mmol/mol) in extract-treated groups, compared to elevated values (61–76 mmol/mol) in diabetic controls. Lipid peroxidation, indicated by MDA, was markedly reduced in treated groups but significantly elevated in diabetic controls. Moreover, antioxidant enzyme activities (GST and SOD) were significantly improved in extract-treated rats relative to diabetic controls, suggesting oxidative stress modulation. Overall, the findings demonstrate that ethanol leaf extract of *Gongronema latifolium* effectively lowers blood glucose and HbA1c, reduces oxidative stress, and enhances antioxidant enzyme activity, supporting its therapeutic potential in the management of type-2 diabetes mellitus

Key Words: Type-2 diabetes, phytochemical, therapeutic targets alloxin rats, anti-diabetic, leaf extract.

Introduction

Diabetes mellitus is a metabolic disease that is usually caused by an absolute or relative insulin deficiency. It has been defined as a fasting venous plasma concentration that is greater than 7.8mmol/l (140mg/dl) or greater than 11.1mmol/l (200mg/dl) two hours after a carbohydrate meal or two hours after ingestion of the equivalent of 75g of glucose even if the fasting concentration is normal (WHO, 2022). Diabetes mellitus has been reported as a leading global health problem and a risk factor for hypertension, kidney failure, retinopathy, neuropathy, impotence, diabetic foot ulcer, stroke and other cardiovascular diseases. All these contribute to high mortality among diabetic patients. In Nigeria, about 11.2 million people have been reported to be living with diabetes mellitus type-2, with prevalence rate of 10.7% (Okolo et al 2021). This very fact has been supported by Nwoko et al (2020), who reported that by the year 2030, the number of diabetic patients may likely be doubled. What this implies is that by the year 2030, more than 20million Nigeria will develop diabetes mellitus type -2 and suffer from the complications associated with it.

The complications arising from diabetes kills more people in Nigeria every year than breast cancer and HIV/AIDs combined together. (Obodo, 2020). If no proactive

measures are taken by way of preventing onset of the disease, the Nigeria workforce will be seriously affected and this may likely impact negatively on productivity and economy of Nigeria as a nation. There are approved oral hypoglycemic agents such as metformins which acts as the first line of pharmacotherapy for type 2 diabetes. Although these agents are often associated with some side effects and have not been absolutely wonderful in the management of type 2 diabetes (Probinake et al 2020). Despite the remarkable achievements in the management of diabetes using synthetic drugs, there has been a renewed interest in medicinal plants due to its efficacy and cost effectiveness. *Gongronema latifolium* being one of the medicinal plants of interest in Nigeria is a leafy green plant that is characterized by its glossy dark green leaves. It is heart shaped with serrated edge and has a slightly bitter and aromatic flavour (Okolo et al 2021). Generally, *Gongronema latifolium* is called utazi in Ibo and arokeke in Yoruba communities (Morebise et al, 2020). Ugochukwu et al, (2020) documented the ethno-medical usage of the plant in man with some evidence of hypolipidemic, hypoglycemic and anti-inflammatory properties. In many situations, it has been part of herbal prescriptions or preparations administer by some African herbalist for treatment of certain health

challenges such as pain infertility, ulcer and hypertension (Schneider et al, 2019).

Materials and Methods

Plant Materials and Authentication

Gongronema latifolium leaves were purchased from local markets within Imo State and the identification and authentication was done by a taxonomist in the Department of Botany and plant Biotechnology of imo state university Owerri.

Preparation of Gongronema Latifolium Leaf Extract

The leaves were dried at 25°C for 30 days and pulverized into powder using an electric blender. The powdered sample (200mg) was soaked in 200ml of distilled water for 24hrs, filtered and freeze dried to obtain the dried extract. Two hundred and fifty milliliter (250ml) of the freeze-dried extract was recommended dose for a 70kg man; since we used experimental rats to get 12.70mg/kg body weight equivalent dose of 70kg man by multiplying and dividing by 2 to get high and low dose.

Experimental Animals

Forty (40) albino rats were acquired from the Department of Animal Production of Michael Okpara University of Agriculture Umudike. The rats were allowed to

acclimatize for two weeks before using them for the study.

Induction of Diabetes

Five grams (5g) of alloxin monohydrate was liquefied in 9% saline and was used to induce diabetes in the rats by simple intraperitoneal injection at a rate of 150mg/kg body weight. Forty-eight (48hrs) hours after the induction, blood samples were collected to determine the fasting blood glucose levels in the rats.

Treatment of Animals with Plant Extract and Metformin

Gongronema Latifolium leaf extract was administered to the rats at a dose of 12.5mg/kg, 25mg/kg, 50mg/kg, 75mg/kg, 100mg/kg, 125mg/kg through oral gavage i.e. through the oesophageal cannula as well as metformin (5mg/kg) to another set of diabetes rats, daily for two weeks.

Grouping of Experimental Animals

- | | |
|----------|---|
| Group A: | Control Group |
| Group B: | Diabetic Control |
| Group C: | diabetic and 5mg of metformin |
| Group D: | diabetic rats and 12.5mg/kg body weight of <i>Gongronema latifolium</i> extent. |
| Group E: | diabetic rats and 25mg/kg body weight of <i>Gongronema latifolium</i> extent. |

- Group F: diabetic rats and 50mg/kg body weight of *Gongronema latifolium* extent.
- Group G: diabetic rats and 75mg/kg body weight of *Gongronema latifolium* extent.
- Group H: diabetic rats and 100mg/kg body weight of *Gongronema latifolium* extent.
- Group I: diabetic rats and 125mg/kg body weight of *Gongronema latifolium* extent.

Collection of Samples

The rats were sacrificed after two weeks of treatment using cervical dislocation. The blood samples were collected in fluoride bottles, while some were collected using needle and syringes and those in syringe were allowed to clot. Thereafter, the blood samples were centrifuged at 3000rpm using a wisperfuge centrifuge. Serum samples collected after centrifugation were used for the analysis.

Determination of Blood Glucose Levels

The blood glucose levels in the different groups of the rats were determined using glucometric as well as oxidase-peroxidase methods. In glucometric method, blood samples were collected from the tips of the rats tail and a drop of the blood was placed on the strip and inserted into the glucometer

machine. Also, the oxidase-peroxidase method as described by Leo et al (2010) was also used. In this method, one milliliter (1ml) of oxidase reagent as well as 1ml of colour reagent was reconstituted with 0.1ml of serum. The sample was allowed to stand for 30mins in water bath and was read at 670nm using spectrophotometer.

Determination of Glycated Haemoglobin

This was determined based on the method described by Habi et al (1979). The blood sample was lysed in order to release the red cells; about 0.1ml of sample was added to 1ml of Fructosyl Peptide Oxidase and was allowed to stand for 30 mins. The colour produced was measured at 500nm using spectrophotometer.

Biochemical Analysis

The serum urea and creatinine were determined using the method as described by Anderson et al (1999) whereas Na⁺, K⁺, Cl⁻ and HCO₃⁻ levels were determined using flame photometric method as described by Anderson et al (1990).

Determination of Super Oxide Dismutase

The super oxide dismutase activity was determined based on the method described by Zelko et al (2003).

Determination of Glutathione Peroxidase

The method described by Kovic et al (2008) was adopted for the determination of glutathione peroxidase activity.

Determination of Glutathione –S-Transferase

Glutathione-S-Transferase activity was measured using the method described by Habib et al (1979).

Malondialdehyde Level Determination

Lipid peroxidation marker was determined by measuring the malandialdehyde level as described by Ohakwe et al (2008).

Mineral Element Analysis

The mineral elements in the samples will be determined by first of all ashing the sample

as described by Osobo et al (1996). The different mineral compositions were determined using atomic absorption spectrophotometric method.

Phytochemical Screening

The different phytochemical fractions of Gongronema Latifolium leaf were isolated using gas chromatographic flame ionization detector as adopted by Imo-c and Uhuegbu (2015).

Statistical Analysis

The data generated were expressed as mean and standard deviation. Values of less than 0.05 ($p < 0.05$) were considered significant.

Results and Discussion

Table 1 Shows The Mean Values Phytochemicals In Aqueous And Ethanol Leaf Extract Of Gongronema Lalifolium.

Parameters	Aqueous Extract	Ethanol Extract
Alkaloids	0.6 ± 0.16	1.2 ± 0.25
Flavonoids	0.3 ± 0.12	1.0 ± 0.16
Phenols	0.6 ± 0.01	1.0 ± 0.02
Saponins	0.9 ± 0.62	1.4 ± 0.92
Sterols	0.4 ± 0.20	0.8 ± 0.88
Terpenoids	0.5 ± 0.10	1.1 ± 0.61
Tannins	0.7 ± 0.06	0.7 ± 0.20

Table 2 Shows the mean values for fasting blood glucose levels before and after alloxin induction.

Parameters	Before Alloxin Induction	After Alloxin
Fasting blood glucose mg/dl	54 ± 0.21	188 ± 0.33
Glycated haemoglobin %	4.1 ± 0.72	8.5 ± 0.31
Fed State Blood Glucose mg/dl	86 ± 0.73	250 ± 1.04

Table 3 Shows the mean and standard deviation values for fasting blood glucose levels in alloxin induced diabetic rats treated with *Gongronema lalifolium* ethanol Leaf Extract at different concentrations.

Groups	IFBG (mg/dl)	FBG after 48hrs Alloxin induction (mg/dl)	FBG after treatment with GLALE (mg/dl)
Control group A	51 ± 0.26	58 ± 2.14	59 ± 1.32
Diabetic Control B	59 ± 1.03	208 ± 3.16	212 ± 2.68
Diabetic and 5mg of metformin	50 ± 2.07	198 ± 2.72	99 ± 1.73
Diabetic and 12.5mg/kg of GLELE	48 ± 1.10	187 ± 3.15	93 ± 2.26
Diabetic and 25mg/kg of GLELE	52 ± 2.13	193 ± 2.75	86 ± 2.88
Diabetic and 50mg/kg of GLELE	45 ± 0.99	184 ± 2.19	47 ± 2.15
Diabetic and 75mg/kg of GLELE	55 ± 1.11	182 ± 1.95	49 ± 2.75
Diabetic and 100mg/kg of GLELE	49 ± 2.11	192 ± 2.15	35 ± 1.10
Diabetic and 125mg/kg of GLELE	53 ± 0.93	206 ± 3.14	32 ± 2.19

Key: IFBG: Initial Fasting Blood Glucose, FBG: Fasting Blood Glucose, LELE: *Gongronema lalifolium* Ethanol Leaf Extract

Table 4 Shows the mean values of Glycated Hemoglobin levels in alloxin induced diabetic rats treated with *Gongronema Lalifolium* Ethanol Leaf Extract.

Groups	IHBAIC (mmol/mol)	IHBAIC after 48hrs Alloxin induction (mmol/mol)	IHBAIC after treatment with GLALE (mmol/mol)
Control Group	40 ± 0.20	37 ± 0.39	30 ± 0.16
Diabetic Group	49 ± 0.06	68 ± 1.77	59 ± 0.19
Diabetic and 5mg of metformin	47 ± 2.11	65 ± 2.19	35 ± 2.17
Diabetic and 12.5mg/kg of GLELE	48 ± 2.16	68 ± 1.99	40 ± 1.88
Diabetic and 25mg/kg of GLELE	48 ± 0.90	61 ± 0.91	30 ± 0.29
Diabetic and 50mg/kg of GLELE	42 ± 0.96	73 ± 0.41	32 ± 0.16
Diabetic and 75mg/kg of GLELE	44 ± 1.62	76 ± 0.71	20 ± 0.65
Diabetic and 100mg/kg of GLELE	47 ± 0.20	70 ± 1.11	19 ± 0.52
Diabetic and 125mg/kg of GLELE	49 ± 3.16	66 ± 2.16	16 ± 0.44

Key: IHBAIC: Initial Glycated Hemoglobin, HBAIC: Glycated Hemoglobin

Table 5 Show the mean values for Urea and Creatinine levels in Alloxin induced diabetic rats treated with *Gongronema lalifolium* Ethanol Leaf Extract.

Groups	Before Treatment		After Alloxin Treatment		After Treatment with GLALE	
	Urea	Creatinine	Urea	Creatinine	Urea	Creatinine
Control Group	13 ± 0.91	0.6 ± 0.01	18 ± 0.25	0.8 ± 1.11	17 ± 0.11	0.9 ± 1.03
Diabetic Group	25 ± 0.73	0.8 ± 0.12	19 ± 0.29	0.7 ± 0.22	16 ± 0.21	1.0 ± 0.93
Diabetic and 5mg of metformin	19 ± 0.22	0.7 ± 0.19	14 ± 0.16	0.5 ± 0.16	10 ± 1.01	1.1 ± 0.77
Diabetic and 12.5mg/kg of GLELE	23 ± 0.61	0.5 ± 0.22	20 ± 0.19	0.7 ± 0.19	19 ± 0.92	0.9 ± 0.60
Diabetic and 25mg/kg of GLELE	17 ± 0.54	0.9 ± 1.22	14 ± 0.18	0.9 ± 0.18	16 ± 0.13	0.6 ± 0.27
Diabetic and 50mg/kg of GLELE	14 ± 0.16	1.0 ± 1.11	12 ± 0.16	0.9 ± 0.12	13 ± 0.94	0.8 ± 1.01
Diabetic and 75mg/kg of GLELE	15 ± 0.20	0.9 ± 0.99	10 ± 0.15	1.0 ± 0.23	12 ± 0.92	0.9 ± 1.01
Diabetic and 100mg/kg of GLELE	12 ± 0.15	1.0 ± 0.48	16 ± 0.40	0.9 ± 0.26	13 ± 1.01	1.2 ± 1.92
Diabetic and 125mg/kg of GLELE	9.0 ± 0.09	1.2 ± 1.01	11 ± 0.17	0.8 ± 1.00	14 ± 1.11	1.1 ± 0.97

Table 6 Shows the mean values for Glutathione– S –Transferase (GST) in alloxin induced diabetic rats after treatment with *Gongronema Lalifolium* Ethanol Leaf Extract.

Groups	GST Before Treatment	GST After 2wks of GLALE
Control Group	480 ± 0.61	495 ± 0.71
Diabetic Group	310 ± 1.96	75 ± 0.66**
Diabetic and 5mg of metformin	360 ± 1.62	299 ± 2.16
Diabetic and 12.5mg/kg of GLELE	385 ± 2.61	390 ± 2.67
Diabetic and 25mg/kg of GLELE	387 ± 1.97	401 ± 2.16
Diabetic and 50mg/kg of GLELE	560 ± 2.20	493 ± 2.26
Diabetic and 75mg/kg of GLELE	409 ± 2.16	422 ± 3.16
Diabetic and 100mg/kg of GLELE	395 ± 1.99	416 ± 2.88
Diabetic and 125mg/kg of GLELE	407 ± 2.16	435 ± 3.16

** : Significant Difference. **Key: GST:** Glutathione– S –Transferase

Table 7 Shows the mean values for Super Oxidase Dismutase (SOD) in alloxin induced diabetic rats after two weeks of treatment with Aqueous Leaf Extract of Gongronema Lalifolium.

Groups	SOD Before Treatment μ/mg protein	SOD After 2wks Treatment with GLALE (μ/mg protein)
Control Group	110 $\pm$ 2.62	102 $\pm$ 0.72
Diabetic Group	96 $\pm$ 0.94	36 $\pm$ 0.16
Diabetic and 5mg of metformin	86 $\pm$ 0.26	94 $\pm$ 0.76
Diabetic and 12.5mg/kg of GLELE	94 $\pm$ 0.36	103 $\pm$ 0.86
Diabetic and 25mg/kg of GLELE	86 $\pm$ 0.26	89 $\pm$ 0.7
Diabetic and 50mg/kg of GLELE	79 $\pm$ 0.66	82 $\pm$ 0.66
Diabetic and 75mg/kg of GLELE	95 $\pm$ 0.95	101 $\pm$ 0.79
Diabetic and 100mg/kg of GLELE	140 $\pm$ 2.06	153 $\pm$ 1.26
Diabetic and 125mg/kg of GLELE	160 $\pm$ 2.09	182 $\pm$ 2.16

Table 8 Shows The Mean Values For Malondialdehyde (MDA) In Alloxin Weeks Of Treatment With Gongronema Latifolium Aqueous Leaf Extract.

Group	MDA Before Treatment (μ mol/L)	MDA After Treatment with GLALE (μmol/L)
Control Group	1.2 $\pm$ 0.66	0.8 $\pm$ 0.11
Diabetic Group	1.0 $\pm$ 0.26	1.7 $\pm$ 0.19
Diabetic and 5mg of Metformin	1.8 $\pm$ 0.11	0.9 $\pm$ 0.22
Diabetic and 12.5mg/kg of GLELE	2.0 $\pm$ 0.64	1.4 $\pm$ 0.26
Diabetic and 25mg/kg of GLELE	2.1 $\pm$ 0.71	1.3 $\pm$ 0.36
Diabetic and 50mg/kg of GLELE	1.0 $\pm$ 0.64	1.4 $\pm$ 0.22
Diabetic and 75mg/kg of GLELE	0.9 $\pm$ 0.71	0.8 $\pm$ 0.71
Diabetic and 100mg/kg of GLELE	1.1 $\pm$ 0.66	0.9 $\pm$ 0.66
Diabetic and 125mg/kg of GLELE	0.9 $\pm$ 0.77	0.7 $\pm$ 0.61

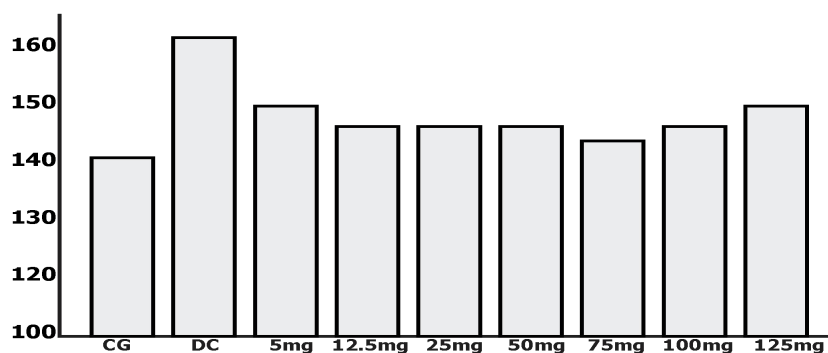


Figure I show the Plasma Sodium levels after treatment with different concentrations of *Gongronema latifolium* Aqueous Leaf Extract.

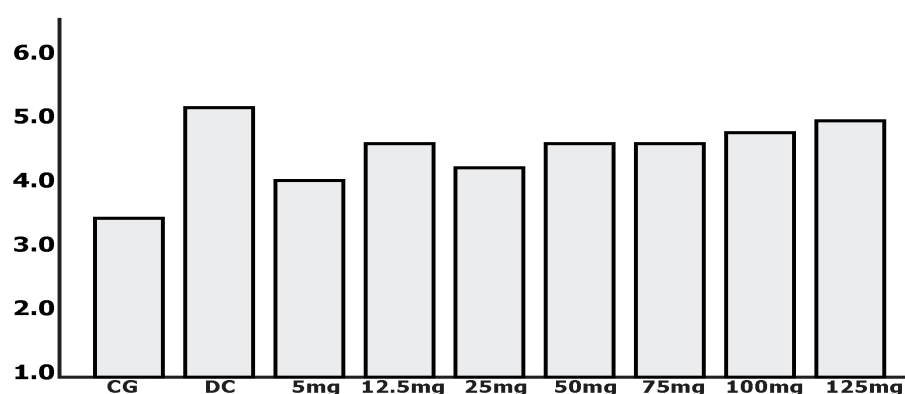


Figure 2 shows the Potassium levels after treatment with the different concentrations of *Gongronema latifolium* Ethanol leaf extract.

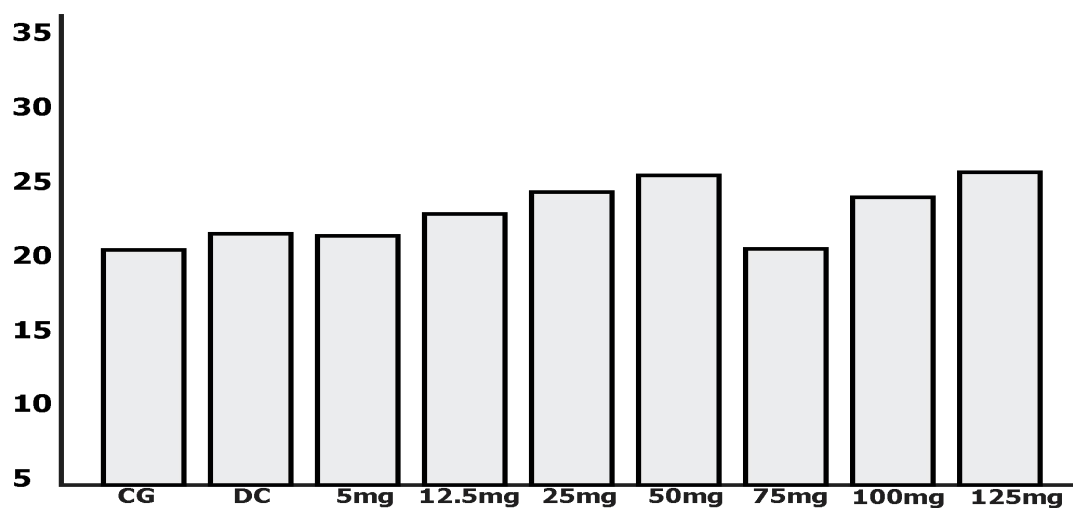


Figure 3 shows the HCO₃⁻ levels in alloxin induced diabetic rats after treatment with *Gongronema latifolium* Ethanol leaf extract.

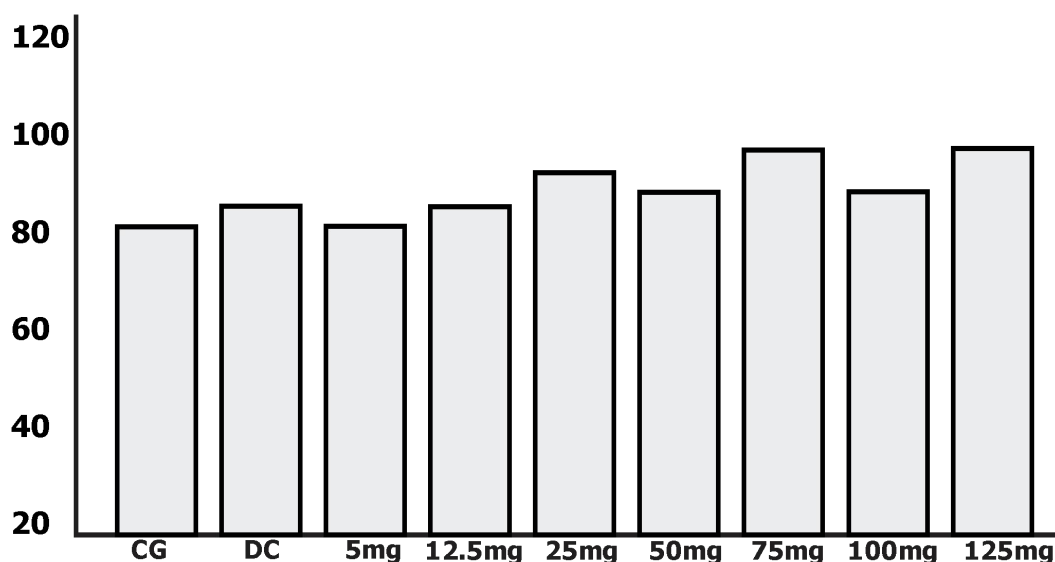


Figure 4 Show the chloride levels after treatment with different concentrations of *Gongronema lalifolium* Ethanol leaf extract.

This study was conducted to determine the potential phytochemicals in locally grown *Gongronema Lalifolium* Aqueous and Ethanol Leaf Extract against therapeutic targets of type-2 diabetes mellitus in alloxin induced diabetic rats. The result of the study revealed the presence of the following Bio-active Compounds like Alkaloids, Flavonoid's, Phenols, Saponins, Sterols, Terpenoids, and Tanins (0.6 ± 0.16 , 0.3 ± 0.12 , 0.6 ± 0.01 , 0.9 ± 0.62 , 0.4 ± 0.22 , 0.3 ± 0.10 , and 0.7 ± 0.26) respectively for aqueous leaf extract, as well as; (1.2 ± 0.25 , 1.0 ± 0.16 , 1.0 ± 0.22 , 1.4 ± 0.92 , 0.8 ± 0.88 , 1.1 ± 0.61 and 0.7 ± 0.20) for ethanol leaf extract. There was a significant difference ($p < 0.25$) in the level of phytochemicals such as Alkaloids, Flavonoids, Saponins and Terpenoids in ethanol leaf extract of *Gongronema lalifolium* when compared

with those of aqueous leaf extract of *Gongronema lalifolium*.

The higher concentrations of most of the phytochemicals from ethanol extract could be due to the fact ethanol is less polar than water which allows it to extract wider range of phytochemicals. It could also be due to its ability to break down cell walls and release bio-active molecules more effectively. From the table 3 above, the result of the study also revealed a significant decrease in the mean values of fasting blood glucose levels in alloxin induced diabetic rats treated with varied concentrations of ethanol leaf extract of *Gongronema Lalifolium* (99 ± 1.73 , 93 ± 2.26 , 97 ± 2.89 , 47 ± 3.15 , 50 ± 2.75 , 35 ± 1.10 and 32 ± 2.19 mg/dl) when compared with those induced with alloxins used to induce diabetes (198 ± 2.72 , 187 ± 2.15 , 193

± 2.75 , 184 ± 2.19 , 182 ± 1.95 , 192 ± 2.15 and 206 ± 2.88 mg/dl) respectively.

The presence of some bio-active compounds like Alkaloids, Phenols, Terpenoids etc., that were isolated in both ethanol and aqueous leaf extract of *Gongronema Lalifolium* could be responsible for the lowering effect on blood glucose levels as recorded in this study. Report by Cho et al (2020) has revealed that Flavonoids such as quercetin can inhibit α – glucosidase which is an enzyme that is responsible for carbohydrate digestions in the small intestine. By inhibiting these enzymes, Flavonoids delay carbohydrate absorption, thereby reducing post prandial glucose level. It has also been reported by Morebise et al (2020), that Flavonoids stimulates insulin release by the B- cells of the pancreatic islets thereby enhancing Glucose in tissues which usually leads to a resultant reduction in the blood glucose levels. According to Okorie et al (2021), the phenol compound in *Gongronema lalifolium* has the ability to reduce blood glucose levels and this could be achieved by inhibiting Glucose-6-phosphatase, an enzyme that is involved in gluconeogenesis.

Also, terpenoid was another very important bio-active compound that was isolated from both aqueous and ethanol leaf extract of *Gongronema lalifolium*. Terpenoids have been known for its blood glucose lowering

effect (Nwoko et al, 2021). It usually acts through activation of Adenosine Monophosphate Protein Kinase (AMPK), thereby enhancing glucose uptake in the muscles at the same time inhibiting glucose production in the liver. Therefore, it is imperative to say that all these bioactive phytochemicals isolated in both aqueous and ethanol leaf extract of *Gongronema lalifolium* may have worked significantly in reducing blood glucose levels in these alloxin induced diabetic rats. As shown in table 4 above, glycated hemoglobin (HBAIC) was determined in rats treated with different concentrations of ethanol extracts of *Gongronema lalifolium* (3.5 ± 2.17 , 40 ± 1.88 , 30 ± 0.29 , 32 ± 0.16 , 20 ± 0.65 , 19 ± 0.52 and 16 ± 0.44) mmol/mol and there was a significant reduction in levels of glycated hemoglobin in rats treated with varied concentrations of *Gongronema lalifolium* ethanol extract, when compared with the results of those that were induced diabetes using alloxin (65 ± 0.19 , 68 ± 1.99 , 61 ± 0.91 , 73 ± 0.41 , 76 ± 0.71 , 75 ± 1.11 , and 66 ± 2.16) mmol/mol. Since elevated levels of glycated hemoglobin signifies poor blood glucose control which can increase the risks and complications associated with diabetes mellitus; therefore, the significant reduction in glycated hemoglobin recorded in this study after treatment with different concentrations of *Gongronema lalifolium* could be attributed to the presence of

bioactive compounds like alkaloids and terpenoids. Also from the table 5 above, the result of the study revealed a normal range of Urea and Creatinine in all the rats treated with ethanol extract of *Gongronema Lalifolium* in all the groups. This result suggests that the plant is safe for human consumption and will not have any adverse effect on the kidneys. The result is also in consonance with what was obtained for the electrolytes (Na^+ , K^+ , Cl^- and HCO_3^-) as shown in figure 1,2,3, and 4. The study revealed serum electrolyte results that were all within normal range. Since there was no alteration in the electrolyte balance, it means that the plant was also safe for human consumption. From table 6 above, the result of the study showed a significant increase in the glutathione-S-transferase (GST) level in all the rats treated with ethanol extracts of *Gongronema lalifolium* except in the case of the diabetic control that was not treated with *Gongronema lalifolium* extract.

The significant increase in the level of GST in the rats treated with ethanol extract could be an indication of an enhanced detoxification and anti-oxidant defense, since GST enzyme plays an important role in protecting the cells from oxidative stress and damage as a result of free radicals. The result of the present study also revealed a significant reduction in the levels of Super Oxidase Dismutase (SOD) in the rats that

served as diabetic control when compared with other groups, as shown in table 7. This reduction in the SOD in diabetic control could be associated with increased oxidative stress usually common among diabetic which usually triggers complications in diabetics. As shown in table 8 above, the result of the study also revealed a significant increase in malondialdehyde (MDA) levels in the diabetic control group when compared with other groups. The significant increase in MDA may have been caused by oxidative stress and lipid peroxidation which is always associated with hyperglycemia. This usually happens whenever the blood glucose level is excessively high leading to an increased production of reactive oxygen species (ROS), which has the capacity to damage the cells. The ROS usually initiates lipid peroxidation which usually stimulates the production of MDA as a biomarker for oxidative stress.

Conclusion

The findings of the study have demonstrated that aqueous and ethanol leaf extract of locally grown *Gongronema lalifolium* has the potentials to reduce blood glucose levels. This fact was established by its ability to regulate multiple therapeutic targets of diabetes mellitus through activation of adenosine monophosphate protein kinase

(AMPK) which enhances glucose uptake in the muscles thereby stimulating the β -cells of the pancreatic islets for increased insulin release and inhibition of glucose-6-phosphatase, an enzyme produced by the liver that enhances gluconeogenesis. All these multiple mechanisms have contributed to the significant reduction in the blood glucose level in the rats. The reduction in the blood glucose level was possible due to the presence of phytochemicals like flavonoids, alkanoids, terpenoids phenols etc. Therefore, the extracts ability to regulate multiple therapeutic targets makes it promising for diabetic treatment and control.

Acknowledgement

We want to acknowledge Tetfund for funding this research with reference number: TETF/DR&G/CE/UNI/UMUAGWO/IBR/2024/VOL.1

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