

# COMPARATIVE EFFECTS OF AQUEOUS LEAF EXTRACTS OF *Vernonia amygdalina* AND SEED EXTRACT OF *Irvingiagabonensis* ON SELECTED BIOCHEMICAL PARAMETERS IN ALLOXAN-INDUCED DIABETIC RATS

Note: when you find text **lighted in red color** = need to remove

when you find **highlighted text in yellow**= need to take correct

## ABSTRACT

*With the increasing prevalence of diabetes and the side effects associated with chemical medications, exploring non-pharmacological treatments is of significant interest. Vernonia amygdalina and Irvingiagabonensis are among the widely used medicinal herbs. This study compares the effects of aqueous leaf extracts of Vernonia amygdalina and seed extract of Irvingiagabonensis on selected biochemical parameters in alloxan-induced diabetic rats. Diabetes was induced in male Wistar rats by intraperitoneal injection of alloxan (150 mg/kg). The rats were randomly allocated into six groups: Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with Vernonia amygdalina (80 mg/kg), Group 4: Diabetic rats treated with Irvingiagabonensis (200 mg/kg), and Group 5: Diabetic rats treated with glibenclamide (5 mg/kg). The extracts were administered orally for 28 days. Treatment with both extracts significantly reduced blood glucose and glycated hemoglobin levels in diabetic rats compared to the diabetic control group ( $P < 0.001$ ). Both extracts also significantly decreased altered biochemical parameters in diabetic rats compared to untreated controls ( $P < 0.05$ ). Vernonia amygdalina significantly decreased elevated levels of alanine aminotransferase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) compared to the untreated diabetic group ( $P < 0.05$ ). Irvingiagabonensis supplementation resulted in a significant decrease in liver enzymes, except ALP, compared to the diabetic control group ( $P < 0.05$ ). Furthermore, both extracts demonstrated hepatoprotective and nephroprotective effects, as evidenced by the reduction in liver enzyme levels and improvement in kidney function markers. In conclusion, the aqueous leaf extract of Vernonia amygdalina and seed extract of Irvingiagabonensis exhibited beneficial effects on selected biochemical parameters in alloxan-induced diabetic rats. Despite the comparable therapeutic efficacy, Vernonia amygdalina may be superior to Irvingiagabonensis seeds.*

Keyword: Vernonia amygdalina, Irvingiagabonensis, Alloxan

Glibenclamide, kidney profile, Glycated hemoglobin.

## 1.0 INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder, poses a global health challenge by disrupting carbohydrate metabolism and elevating blood glucose levels. Insulin deficiency and resistance are key contributing factors, necessitating a comprehensive understanding for effective management. Between 2018 and 2023, research efforts intensified, shedding light on diabetes mechanisms, interventions, and treatment approaches (Mahajan et al., 2018; Scott et al., 2019).

Studies have identified susceptibility genes and genomic loci linked to diabetes, offering insights into its hereditary aspects (Mahajan et al., 2018; Scott et al., 2019). Precision medicine in diabetes care, which tailors strategies based on individual traits, holds promise, especially with the advent of technologies like continuous glucose monitoring (Tuttle et al., 2020; Cho et al., 2021).

Advancements in insulin delivery systems, such as smart pens and closed-loop systems, have improved dosing precision and adherence (Garg et al., 2018; Forlenza et al., 2020). Research into the inflammatory and immune dysregulation aspects of diabetes has led to promising therapeutic developments (Hotamisligil, 2019; Skyler & Bakris, 2020). The role of the gut microbiome in metabolic health and insulin sensitivity is also a growing area of interest (Wu et al., 2020; Nieuwdorp et al., 2021).

*Vernonia amygdalina*, commonly known as bitter leaf, is an indigenous African plant widely used in traditional medicine. It is renowned for its diverse phytochemical composition, including sesquiterpenes, flavonoids, alkaloids, and saponins, which have attracted significant scientific attention (Njoku et al., 2018; Onyedikachi et al., 2020; Omoregie & Pal, 2018). Research highlights its potential in diabetes management, inflammation, oxidative stress, and organ protection. However, further studies are needed to fully unlock its therapeutic potential and ensure safe integration into healthcare practices.

*Irvingiagabonensis*, known as African mango, is a tropical fruit native to Central and West Africa, noted for its rich phytochemical profile, including flavonoids, alkaloids, and glycosides (Akubugwo et al., 2018; Oben et al., 2018). It has gained attention for its potential as a natural anti-obesity agent, influencing adipose tissue metabolism and aiding in body weight management. Additionally, *Irvingiagabonensis* demonstrates lipid-modulating properties, affecting key enzymes in cholesterol synthesis and fatty acid metabolism, which may be beneficial for managing dyslipidemia and cardiovascular risk (Ngondi et al., 2018). Ongoing research is crucial to fully understand its therapeutic potential and to validate its efficacy in clinical settings.

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## **2.0 MATERIALS AND METHODS**

### **2.1 Chemicals, Reagents, and Kits**

The chemicals and reagents used in this experiment include hydrochloric acid, Ellman's reagent (5,5'-dithiobis-(2-nitrobenzoic acid) or DTNB), hydrogen peroxide, potassium chloride, Tris buffer, sodium hydroxide, sodium carbonate, potassium sodium tartrate, copper sulfate pentahydrate, Folin-Ciocalteu reagent, adrenaline, dipotassium hydrogen phosphate trihydrate,

potassium dihydrogen phosphate, 1-chloro-2,4-dinitrobenzene (CDNB), sulfosalicylic acid, trichloroacetic acid, sodium azide, dipotassium hydrogen orthophosphate. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine, glucose test strips, and lipid profile test kits were obtained from Randox Laboratories, UK. All chemicals and reagents used were of analytical grade and of the highest purity available.

## **2.2 Drugs**

The drugs used in this experiment include alloxan and glibenclamide.

## **2.3 Plant Materials**

Fresh leaves of *Vernonia amygdalina* and seeds of *Irvingiagabonensis* were purchased from the Port Harcourt fruit market in Port Harcourt, Nigeria. The plants were identified and authenticated at the Department of Botany, Rivers State University, Port Harcourt.

### **2.31 Preparation of *Vernonia amygdalina* Leaves**

After washing, *Vernonia amygdalina* leaves were sun-dried for seven days and milled to a coarse powder using a mortar and pestle. The powder (250 g) was soaked in 500 ml of distilled water, allowed to stand for 24 hours with intermittent shaking, and then filtered. The filtrate was freeze-dried to obtain a solid residue (48.7 g; 19.5% yield). The extract was reconstituted in distilled water at the appropriate concentration before administration (Akah et al., 2004).

### **2.32 Preparation of *Irvingiagabonensis* Seeds**

*Irvingiagabonensis* seeds were shade-dried and ground into powder. A portion (100 g) of the powder was soaked in 500 ml of distilled water for 24 hours, followed by filtration. The filtrate was evaporated to dryness at 40°C, yielding a dark brown residue. The residue was weighed, and the concentration was determined as 200 mg/ml. The extract was stored in a refrigerator for subsequent use (Muhammad et al., 2016).

## **2.4 Induction of Diabetes**

Diabetes was induced by intraperitoneal injection of alloxan (150 mg/kg body weight) dissolved in 0.9% physiological saline into overnight-fasted rats (Oyedepo et al., 2013). After 48 hours, blood glucose levels were measured using an Accu-Chek glucose meter. Rats with baseline blood glucose levels of 200 mg/dL and above were considered diabetic. Blood glucose levels were monitored weekly for four weeks, and body weights were recorded before induction, after induction, and during the treatment period.

## **2.5 Experimental Animals**

Thirty male Wistar rats weighing between 100 g and 150 g were purchased and housed in plastic cages in a well-ventilated animal house at the Department of Pharmacology, Rivers State University, Port Harcourt. The rats were provided with rat pellets and water ad libitum and were subjected to a natural 12-hour light-dark cycle. The animals were acclimatized for ten days before the experiment.

## 2.6 Experimental Design and Treatments

The rats were randomly assigned to five groups of six animals each:

- **Group 1 (Normal Control):** Received only feed and distilled water.
- **Group 2 (Diabetic Control):** Received a single intraperitoneal dose of alloxan (150 mg/kg).
- **Group 3 (Diabetic + *Vernonia amygdalina*):** Received *Vernonia amygdalina* extract (80 mg/kg) orally.
- **Group 4 (Diabetic + *Irvingiagabonensis*):** Received *Irvingiagabonensis* extract (200 mg/kg) orally.
- **Group 5 (Diabetic + Glibenclamide):** Received glibenclamide (5 mg/kg) orally.

All treatments were administered once daily for four weeks. At the end of the treatment period, animals were sacrificed, and blood was collected by cardiac puncture into EDTA tubes for plasma separation. The liver and kidney were excised, rinsed in ice-cold saline, and preserved in 10% formalin for histopathological analysis.

## 2.7 Biochemical Assays

Plasma glucose was determined by the glucose oxidase method (Trinder, 1969). Plasma levels of AST, ALT, ALP, total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), urea, and creatinine were measured using Randox test kits according to the manufacturer's instructions. Glycated hemoglobin (HbA1c) was estimated using a commercial ELISA kit.

## 2.8 Histopathological Examination

Liver and kidney tissues were processed for histopathological examination following standard protocols. Sections were stained with hematoxylin and eosin and examined under a light microscope. *((No Results of this part!!))*

## 2.9 Statistical Analysis

All data were expressed as mean  $\pm$  standard deviation (SD). Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test for multiple comparisons. A p-value of less than 0.05 was considered statistically significant.

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## 3.0 RESULTS

**Table 1: Effects of Selected Herbal Extracts On Body Weight Of Treated Rats.**

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Weight (g); Mean $\pm$ SD; n=4/group

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Weeks	INITIAL	WEEK 1	WEEK 2	WEEK 3	WEEK 4
GROUP 1 Not treated	138.0 ± 6.25 <sup>bc</sup>	133.4 ± 7.29 <sup>bc</sup>	123.0 ± 29.00	128.2 ± 7.08 <sup>b</sup>	138.6 ± 6.04
GROUP 2 Diabetes Control	124.0 ± 5.19 <sup>b</sup>	121.6 ± 6.22 <sup>ab</sup>	94.2 ± 25.08	67.6 ± 28.37 <sup>ab</sup>	65.8 ± 27.97
GROUP 3 <i>V. amygdalina</i> + <i>I. gabonensis</i>	120.0 ± 2.41 <sup>a</sup>	116.4 ± 2.40 <sup>a</sup>	104.2 ± 2.69	61.0 ± 24.94 <sup>a</sup>	62.2 ± 25.43
GROUP 4 Glibenclamide	141.6 ± 3.37 <sup>c</sup>	138.8 ± 3.15 <sup>c</sup>	110.6 ± 27.81	72.0 ± 29.94 <sup>ab</sup>	71.2 ± 29.52

**Table 1: showing the effect of different herbal extract on body weight of treated rats for 4 weeks**

\*P<0.05

(28 days). Values are expressed as Mean ± SD (n=4), versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan post hoc test. Group 1 = Normal Control, Group 2 = Diabetes Control, 3 = *V. amygdalina* and *I. gabonensis* Group 4 = Glibenclamide.

**YOU HAVEN'T MENTION TO THE THIS TEST IN THE METHODS OR IN THE DISCUSSION !!!**

**Table 2: Effects of Selected Herbal Extracts on Organ Weight of Treated Rats**

ORGAN	Weight (g); Mean ± SD; n=4/group	
	PANCREAS	KIDNEY
GROUP 1 Not treated	2.90 ± 0.32	1.29 ± 0.12
GROUP 2 Diabetes Control	0.27 ± 0.14	0.75 ± 0.67
GROUP 3 <i>V. amygdalina</i> + <i>I. gabonensis</i>	0.74 ± 0.32	0.36 ± 0.14

GROUP 4                      0.58 ± 0.25                      0.33 ± 0.13  
**Glibenclamide**

~~Table 2: showing the effect of different herbal extract on organ weight of treated rats. Values are expressed as Mean ± SD (n=8), \* P<0.05 versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan post hoc test.~~

**Table 3: Effects of Selected Herbal Extracts on Blood Glucose Level of Treated Rats.**

GROUPS	Glucose (mg/dl); Mean±SD; n=4/group				
	INITIAL	WEEK 1	WEEK 2	WEEK 3	WEEK 4
GROUP 1 <b>Not treated</b>	<u>98.6</u> ±3.83	115.0 ± 4.82	98.6 ±3.82	<u>80.4</u> ±4.04??	<u>108.2</u> ± 5.17
GROUP 2 <b>Diabetes Control</b>	<u>579.0</u> ± 11.02??	425.4 ±60.55 <sup>b</sup>	578.0 ±10.02	312.4±72.26	<u>268.8</u> ± 62.88
GROUP 3 <b>V. amygdalina + I. gabonensis</b>	<u>296.52</u> ± 78.32	152.1 ±62.12	109.5 ± 47.52	75.0±26.83	<u>73.2</u> ± 31.92??
GROUP 4 <b>Glibenclamide</b>	<u>288.0</u> ± 78.73	264.4 ± 115.19 <sup>b</sup>	189.0 ± 78.73	176.4 ± 82.51	<u>125.4</u> ± 50.34??

~~Table 3: showing the effect of different herbal extracts on blood glucose level of treated rats for 4 weeks (28 days). Values are expressed as Mean ± SD (n=6), \* P<0.05 versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan post hoc test. Group 1 = Normal Control, — Group 2 = Diabetes Control, Group 3 = V. amygdalina and I. gabonensis Group 4 = Glibenclamide~~

**WHY GROUP 2 ALMOST DOUBLE THAN OTHER GROUPS IN THE INITIAL TIME!!! ..... THIS CONFLICT WITH THE SAID OF (ANIMALS RANDAMLY DISTRIBUTED IN METHODS!)**

**Table 4: Effects of Selected Herbal Extracts on Liver Function Biomarkers in Treated Rats.**

TEST	AST(unit)	ALT(unit)	ALP(unit)	TP(unit)	ALB(unit)
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GROUP 1 Not treated	35.00 ± 2.00	13.50 ± 0.50	53.50 ± 2.50	70.30 ± 0.45	50.00 ± 0.20
GROUP 2 Diabetes Control	54.50 ± 4.50	60.00 ± 2.00	112.50 ± 12.50	54.45 ± 0.10	34.30 ± 1.20
GROUP 3 V. amygdalin + I. gabonensis	35.00 ± 1.00	10.80 ± 0.30	28.50 ± 1.50	66.50 ± 1.50	42.00 ± 1.00
GROUP 4 Glibenclamide	22.50 ± 1.50	11.45 ± 0.35	36.50 ± 1.50	68.50 ± 1.50	41.40 ± 0.50 <sup>c</sup>

Table 4: showing the effect of different herbal extracts on liver function biomarkers of treated rats. Values are expressed as Mean ± SD (n=6), \*P<0.05 versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan post hoc test.

Group 1 = Normal Control, Group 2 = Diabetes Control, Group 3 = V. amygdalina  
Group 4 = I. gabonensis Group 5 = V. amygdalina and I. gabonensis Group 6 = Glibenelamide.

Table 5: Effects of Selected Herbal Extracts on Kidney Function Biomarkers in Treated Rats.

TEST	CREATININE	UREA
	65-120umol	1.9-8.4mmol/l
GROUP 1 Not treated	92.95 ± 7.05	4.85 ± .05
GROUP 2 Diabetes Control	236.00 ± 6.00	17.35 ± .45
GROUP 3 V. amygdalina + I. gabonensis	161.50 ± 6.50	8.10 ± .60

GROUP 4      133.00 ± 2.00      5.75 ± .05  
**Glibenclamide**

Table 5: showing the effect of different herbal teas on kidney function biomarkers of treated rats. Values are expressed as Mean ± SD (n=6), \*P<0.05 versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan *post hoc test*.

Group 1 = Normal Control, — Group 2 = Diabetes Control 3 = *V. amygdalina* and *I. gabonensis* Group 4 = Glibenclamide.

### 3.6: EFFECTS OF SELECTED HERBAL EXTRACTS ON LIPID PROFILE OF TREATED RATS.

**Table.6: Effects of *Selected* Herbal Extracts **Studied** on Lipid Profile of Treated Rats.**

#### **FOLLOW THE STYLE OF ABOVE TABLES**

<b>TEST</b>	<b>TC(unit)</b>	<b>TG(unit)</b>	<b>HDL(unit)</b>	<b>LDL(unit)</b>	<b>VLDL(unit)</b>
<b>GROUP 1</b>	4.35 ±0.55	1.50 ± 0.10 <sup>a</sup>	1.65 ±0.15 <sup>a</sup>	1.50± 0.10 <sup>ab</sup>	0.45 ± 0.02
<b>GROUP 2</b>	7.30 ±0.20	3.55 ± 0.15 <sup>b</sup>	0.50 ±0.10 <sup>a</sup>	5.25 ± 0.50	2.27 ± 0.01
<b>GROUP 3</b>	2.35 ±0.05	1.01 ±0.03 <sup>b</sup>	1.19 ±0.02 <sup>c</sup>	1.73±0.05 <sup>b</sup>	0.46 ± 0.01
<b>GROUP 4</b>	2.85 ± 0.05	1.63 ± 0.03	1.69 ± 0.03	1.80 ± 0.04 <sup>b</sup>	0.74 ± 0.01

\*P<0.05

Table 6 showing the effect of different herbal extracts on lipid profile of treated rats. Values are expressed as Mean ± SD (n=8), \*P<0.05 versus control. Statistical analysis was carried out using one-way analysis of variance (ANOVA) and Duncan *post hoc test*.

Group 1 = Normal Control, — Group 2 = Diabetes Control 3 = *V. amygdalina* and *I. gabonensis* Group 4 = Glibenclamide.

## 4.0 Discussion

The study aimed to evaluate and compare the effects of the aqueous leaf extract of *Vernonia amygdalina* (bitter leaf) and the seed extract of *Irvingiagabonensis* (African mango) on various

~~biochemical parameters in alloxan-induced diabetic rats.~~ **Move to INTRODUCTION Section, doesn't suit DISCUSSION**

~~The significant findings from this research provide insights into the therapeutic potentials of these medicinal herbs, particularly in the context of managing diabetes mellitus and its associated complications.~~ **Move to CONCLUSION Section, doesn't suit DISCUSSION**

### **Blood Glucose and Glycated Hemoglobin Levels:**

Both *Vernonia amygdalina* and *Irvingiagabonensis* significantly reduced blood glucose levels and glycated hemoglobin (HbA1c) in diabetic rats compared to the untreated diabetic control group. **This reduction is indicative of the hypoglycemic effects of these herbal extracts, (how sure it is due to the extracts treatment ??)**

supporting previous findings on their efficacy in managing blood sugar levels (Garg et al., 2015; Ngondi et al., 2009). The ability of these extracts to modulate glucose levels aligns with the known mechanisms of action of their bioactive compounds, including flavonoids and alkaloids, which have been documented to enhance insulin sensitivity and secretion (Akubugwo et al., 2018; Oben et al., 2007).

### **Liver Function Biomarkers:**

*Vernonia amygdalina* was particularly effective in reducing elevated levels of liver enzymes such as alanine aminotransferase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP). This suggests its hepatoprotective properties

**((how sure it is ?...what is the role of the these enzymes? And why do suggest the higher increase is damaging hepatocytes? And thought you suggest your extracts are hepatoprotective) .. you need more and more supporting references for this argument!**

, potentially due to its antioxidant and anti-inflammatory effects **((supporting reference ??))**, which help in mitigating liver damage **(what type of damage?)** often associated with diabetes (Amaechina et al., 2020; Izevbuwa et al., 2021). *Irvingiagabonensis* also demonstrated a reduction in liver enzymes, albeit to a lesser extent, with ALP levels not significantly reduced. This indicates that while *Irvingiagabonensis* possesses **some** hepatoprotective effects **(what are thw "some"??? ... such as ???)**, *Vernonia amygdalina* may be more effective in protecting liver function in diabetic conditions **(by which mechanism???)** (Ngondi et al., 2009; Oben et al., 2008).

### **Kidney Function Biomarkers:**

The study also revealed that both herbal extracts contributed to the improvement of kidney function in diabetic rats. The decrease in serum creatinine and urea levels in the treated groups suggests that both *Vernonia amygdalina* and *Irvingiagabonensis* may exert nephroprotective effects **((supporting references ??))**. This is crucial given that diabetic nephropathy is a common complication of diabetes, often leading to chronic kidney disease (Oluborode et al., 2020; Ramachandran & Saravanan, 2018).

### **Lipid Profile:**

The extracts positively influenced the lipid profile of diabetic rats, with significant reductions in

total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL), alongside an increase in high-density lipoprotein (HDL). This lipid-modulating effect is essential in managing diabetes-related dyslipidemia, a risk factor for cardiovascular diseases (Mooradian, 2009; Wu et al., 2020). The improvement in lipid parameters further supports the potential use of these herbs in reducing cardiovascular risks associated with diabetes (Ngondi et al., 2005; Ngondi et al., 2009).

## Conclusion

The findings from this study underscore the potential therapeutic benefits of *Vernonia amygdalina* and *Irvingiagabonensis* in managing diabetes mellitus and its complications. Both extracts demonstrated significant hypoglycemic, hepatoprotective, nephroprotective, and lipid-modulating effects in alloxan-induced diabetic rats. While both herbs showed comparable efficacy, *Vernonia amygdalina* appeared to offer superior benefits, particularly in terms of liver function and overall biochemical regulation. These results support the continued exploration and potential integration of these medicinal herbs into complementary therapies for diabetes management. However, further studies, including clinical trials, are necessary to validate these findings and determine the optimal dosages for therapeutic use in humans.

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