

## *In-Vivo* Oral and Intraperitoneal Administration of Extract from *Vernonia lasiopus*

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### Abstract

Diabetes mellitus in Kenya is a major health concern as it is known to result in mobility, mortality, and long-term complications. Conventional drugs used in the management of diabetes mellitus are unavailable, expensive, and have numerous side effects. *Vernonia lasiopus* plant has a folkloric usage in diabetes mellitus management though its efficacy needs to be evaluated scientifically. This study therefore aimed at establishing *in vivo* antihyperglycemic effect of aqueous leaf extract from *Vernonia lasiopus* in alloxan-induced diabetic male albino mice. Eight groups of mice each group having five mice were used in the study. The plasma sugar lowering effect was monitored after intraperitoneal and oral administration of *Vernonia lasiopus* extract at doses of 25, 48.4, 93.5, 180.9 and 350 mg/kg body weight. The treatment effects of extracts were compared with the positive controls (insulin and glibenclamide treated for intraperitoneal and oral routes respectively). Standard procedures were used to determine the phytochemicals present in the extracts. ANOVA and post-ANOVA was used to analyze the data collected. The results of the study showed that the aqueous leaves extract at all the five doses administered demonstrated antihyperglycemic effect in a dose independent manner. The phytochemical results showed the presence of phenols, tannins, alkaloids, and flavonoids. The antidiabetic effects shown by the plant extract could be due to the phytochemicals present. *Vernonia lasiopus* aqueous leaves extract has antidiabetic effects and the study therefore recommends its folkloric use in management of diabetes mellitus.

**Keywords:** Diabetes mellitus; Aqueous extracts; Hypoglycemic activity; *Vernonia lasiopus*; Glibenclamide

### Abbreviations:

IU: Insulin units; SD: Standard Deviation; SPSS: Statistical Package of Social Sciences; ANOVA: Analysis of variance.

### Introduction

Chronic hyperglycemia is a characteristic of diabetes mellitus. Diabetes mellitus is as a result of defective insulin secretion, a defect in insulin action or both [1]. About 382 million people worldwide were estimated to be diabetic in 2014 but the number may rise to more than 592 million people in 25 years' time [2]. Causes of diabetes mellitus are deficiency of insulin due to insufficient insulin production by pancreas or body tissues resistant to insulin. This leads to a high glucose level in the blood [3]. Diabetes mellitus is known to be caused by autoimmune destruction of  $\beta$ -cell of pancreases leading to insulin insufficiency for type 1 diabetes mellitus. Cause of type 2 diabetes mellitus is a combination of genetic factors which leads to impaired insulin production and resistance to insulin. Environmental factors such as overeating, obesity, stress, lack of exercise and advanced age are known to cause Type II diabetes mellitus [4]. Characteristics of diabetes mellitus are polyuria (excess urine production), polydipsia (thirst), polyphagia (constant feeling of hunger), vision changes, loss of weight, and fatigue [5]. Long-term high blood sugar level causes microvascular and macrovascular complications [6]. The complications are nephropathy, retinopathy, cardiovascular disorders and neuropathy [4]. Diagnosis of diabetes mellitus is by several fasting

blood glucose levels  $\geq 7.0$  mmol/L (126 mg/dl) or postprandial glucose at 2 hours of values  $\geq 11.1$  mmol/L (200 mg/L) [7].

Diabetes mellitus is managed by insulin injection, oral hypoglycemic agents, exercise, acupuncture, proper diet [8]. The conventional drugs such as insulin and oral hypoglycemic agents are unavailable, have numerous side effects and are expensive [9]. The growing interest in folkloric sources is due to numerous side effects as a result of conventional hypoglycemic drugs [10]. Herbal preparations provide valuable sources for chemicals of great importance in medicine and agriculture [11]. Many pharmaceuticals conventional drugs have natural plant origins. An example is metformin which is obtained from *Galega officinalis*, which is a common folkloric remedy for diabetes mellitus [12,13].

Approximately 400 plants are demonstrated to have a hypoglycemic effect [14]. The extract from some herbs only relieves the symptoms and prevent the complication of diabetes mellitus, while others help in overcoming insulin resistance and also help in regeneration of  $\beta$ -cells of pancreas [15]. This study provides the knowledge that supports the use of *Vernonia lasiopus* in the diabetes mellitus management. The *Vernonia lasiopus* samples used were collected from Gilgil sub-county of Nakuru county Kenya.

### Material and Methods

#### Collection of plant leaves

The study was carried out at Kenyatta University in 2016. Leaves of *Vernonia lasiopus* were obtained from the natural habitat. The collection was guided by the reports from local herbalists. The plant

was identified by a taxonomist at the Kenya National Museum Herbarium. The leaves were dried at room temperature for about four weeks until they attained a constant dry weight. Dried leaves were ground with an electric mill and the powder stored in air-tight closed containers away from direct sunlight.

### Preparation of aqueous extract

One hundred grams of the leaves powder was extracted in distilled water at 60°C using a metabolic shaker for six hours. The mixture was then allowed to cool then decanted. The suspension was then filtered over folded cotton gauze in a filter funnel into a dry conical flask. The filtrate was then lyophilized for 72 hours to obtain the freeze-dried samples that were weighed and stored in air-tight containers at -20°C.

### Hyperglycemia induction and experimental design

Four weeks old Male White Albino mice weighing 23-27 g were involved in the study. The mice were housed at Kenyatta University and were fed on rodent pellets and water. The mice were fasted for between 8-12 hours though allowed access to water during the experiment. Diabetic state was induced by intraperitoneal administration of 186.9 milligrams per kilogram body weight of 10% alloxan monohydrate. The control group was administered with normal saline intraperitoneally. The mice were then allowed to stay for 48 hours after administering alloxan monohydrate and then their blood sugar level was measured using a glucometer. Diabetic mice were considered to be those with blood glucose level >11.1 mmol/L or >2000 mg/L and were considered for subsequent experiments.

The mice were assigned into eight groups each having five animals in the experiment. Group I normal control (orally administered with 0.1 ml of physiological saline) Group II negative control (diabetic mice orally administered with 0.1 ml of physiological saline). Group III positive control (diabetic mice orally administered with 200 mg/kg body weight of Glibenclamide which the reference drug). The rest of the groups IV, V, VI, VII, and VIII were orally administered with 25, 48.4, 93.5, 180.9, and 350 mg/kg body weight, respectively of plant extracts (experimental groups). This administration design was then repeated by intraperitoneal route but the reference drug for the intraperitoneal route was 1 IU/kg body weight in 0.1 ml saline.

### Blood sampling, glucose concentration, half-life and rate constant determination

The tail of the mice was sterilized with 10% alcohol nibbed and a drop of blood squeezed into the glucometer strip. The same procedure was repeated after two hours for 10 hours that is at 2, 4, 6, 8 and 10 and also the glucose was measured at 24 hours. The rate constant (k) was obtained after plotting natural logarithm concentration of plasma sugar level against time in hours (the first four hours). The plotted points gave the pseudo-first order rate constant ( $k/2.303$ ). The constant was indicated by the point at which the straight line intersects with the natural log of blood glucose concentration (showing the original blood plasma concentration before administration of the drug) [16]. Substituting the rate constant (k) in the following formula,  $t_{1/2} = 0.693/k$  was used to calculate half-life. From the formula  $t_{1/2}$  is the time taken for the plasma glucose level to reduce by half [17]. The drug dose to be administered after certain duration of time was determined by use of exponential decay equation [18].

### Determination of phytochemicals

The phytochemicals present in aqueous leaves extract of *Vernonia lasiopos* (saponins, flavonoids, alkaloids, sterols, and tannins) were determined using standard procedures [19,20].

### Data management and statistical analysis

Data collected was entered in Microsoft Excel, cloned and then analysed using Statistical Package of Social Sciences (SPSS). The results were expressed as Mean  $\pm$  standard deviation (SD) of the number of animals used in a group. Analysis was done using ANOVA and post-ANOVA which enabled to make comparison of the groups (normal control, negative control, positive control and extract treated groups at the five dose levels). The significant level was considered at  $p \leq 0.05$ .

### Effects of administration of *Vernonia lasiopos* extract on blood glucose levels

Administration of aqueous of *Vernonia lasiopos* extracts orally at 25, 48.4, 93.5, 180.9, and 350 mg/kg body weight to diabetic mice reduced blood plasma level significantly as from the second to the eighth hour in a dose independent manner. The percentage reduction in blood sugar level by the extract as at the second hour was 74.7%, 62.9%, 67.2%, 60.0% and 69.7%, respectively, while that of glibenclamide treated diabetic animals decreased to 66.5% within the same hour (Figure 1). As at the second hour the extract lowered blood glucose levels but not to normal levels ( $^d p < 0.05$ ). The blood sugar lowering effect was however registered with respect to positive control group ( $^a p < 0.05$ ) (Table 1).

At the fourth hour, the percentage plasma sugar lowering effect observed was 56.5%, 45.5%, 46.7% 48.1% and 51.2%, respectively at five doses administered, while the positive control group plasma sugar levels decreased to 49.0% at that hour. At hour six the extract doses lowered plasma sugar level to 48.6%, 32.6%, 31.0%, 38.7% and 37.8%, respectively, while the positive control cohort plasma sugar level reduced to 38.3%. The extract of *Vernonia lasiopos* decreased blood glucose level at this hour to normal ( $^d p > 0.05$ ). The extract dose of 180.9 milligrams per kilogram body weight lowered blood glucose level effectively as glibenclamide at the 6<sup>th</sup> hour ( $^b p < 0.05$ ). Similar results on plasma glucose decreasing effect was shown at the eighth hour where the five doses extract lowered blood sugar level in a manner comparable to glibenclamide (31.7%). The percentage blood sugar lowering effect were 42.8%, 28.0%, 25.4%, 30.9% and 29.6%, respectively (Figure 1).

Intraperitoneal administration of extract of *Vernonia lasiopos* to diabetic mice at five doses (25, 48.4, 93.5, 180.9, and 350 mg/kg body weight) showed significant reductions in blood glucose level as at second hour to the eighth hour in a manner not related to the dose administered. The percentage reductions in the plasma glucose level by the second hour in the diabetic mice were 51.9%, 39.3%, 44.1%, 49.2% and 52.5%, respectively, while the positive control group (Insulin treated diabetic mice) registered 40.9% blood sugar decrease by the second hour (Figure 2). The doses however reduced the blood sugar level significantly compared to negative control (diabetic mice administered with normal saline) ( $^A p < 0.05$ ) (Table 1).

The percentage reductions by the five doses at the 4<sup>th</sup> hour was 41.1%, 31.9%, 37.3% 36.0% and 36.8%, respectively, while the positive control (insulin treated diabetic mice) showed 37.1% decrease in blood

sugar level at the same hour. The extract, however, decreased plasma glucose to normal levels ( $C_p > 0.05$ ). At the sixth hour, the extract lowered blood glucose levels by 32.3%, 23.6%, 30.5%, 26.1% and 37.5%, respectively, while the positive control group plasma glucose levels decreased to 35.6%. By the sixth hour the aqueous extract of *Vernonia*

*lasiopus* at 93.5 mg/kg decreased blood glucose level effectively as insulin ( $B_p < 0.05$ ). Similar trend was observed in the eighth hour where the five doses decreased blood glucose levels lower than insulin (33.0%). The percentage decrease in plasma sugar levels were 29.8%, 20.9%, 26.4%, 21.9% and 23.7%, respectively (Figure 2).

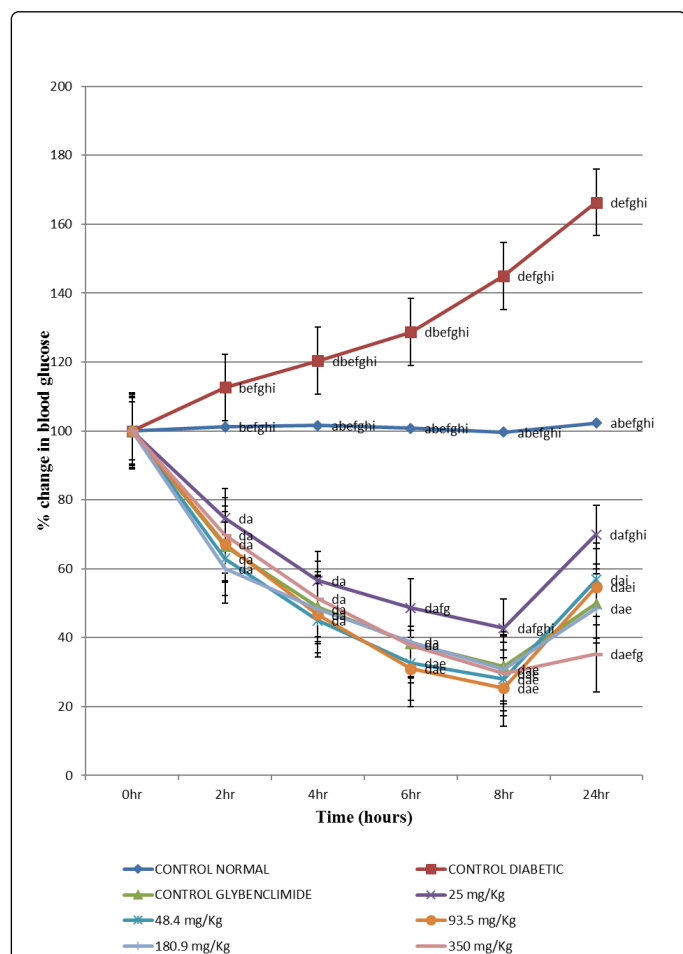
Treatment	Route	Levels of Glucose at Varying Times (mmol/L)					
		0 hour	2 hours	4 hours	6 hours	8 hours	24 hours
Normal control	IP	5.18 ± 0.20 <sup>ABDEFGH</sup>	5.20 ± 0.03 <sup>A</sup>	5.16 ± 0.02 <sup>A</sup>	5.18 ± 0.04 <sup>A</sup>	5.16 ± 0.02 <sup>AG</sup>	5.24 ± 0.02 <sup>ADE</sup>
	Oral	5.18 ± 0.02 <sup>abefghi</sup>	5.20 ± 0.03 <sup>abefghi</sup>	5.16 ± 0.02 <sup>abef</sup>	5.18 ± 0.04 <sup>a</sup>	5.16 ± 0.02 <sup>a</sup>	5.24 ± 0.02 <sup>abefg</sup>
Negative control	IP	13.90 ± 1.28 <sup>C</sup>	15.10 ± 1.29 <sup>CBDEFGH</sup>	16.42 ± 1.10 <sup>CBDEFGH</sup>	17.84 ± 1.16 <sup>CBDEFGH</sup>	19.06 ± 1.13 <sup>CBDEFGH</sup>	22.62 ± 1.06 <sup>CBDEFGH</sup>
	Oral	13.42 ± 1.32 <sup>befghid</sup>	15.12 ± 1.20 <sup>dbefghi</sup>	17.42 ± 1.11 <sup>dbefghi</sup>	18.84 ± 1.18 <sup>dbefghi</sup>	19.08 ± 1.14 <sup>dbefghi</sup>	22.80 ± 1.12 <sup>dbefghi</sup>
Positive control (insulin)	IP	15.78 ± 1.26 <sup>C</sup>	6.46 ± 0.29 <sup>CA</sup>	5.86 ± 0.24 <sup>A</sup>	5.62 ± 0.20 <sup>A</sup>	5.20 ± 0.14 <sup>AEG</sup>	6.90 ± 0.16 <sup>AD</sup>
Positive control (glibenclamide)	Oral	16.42 ± 1.38 <sup>aefghi</sup>	10.92 ± 0.96 <sup>efghi</sup>	8.04 ± 0.45 <sup>efghi</sup>	6.28 ± 0.34 <sup>defghi</sup>	5.20 ± 0.11 <sup>defghi</sup>	8.18 ± 0.53 <sup>efgh</sup>
<b>Extract dose (mg/kg body weight)</b>							
25	IP	13.88 ± 0.48 <sup>C</sup>	7.20 ± 0.55 <sup>A</sup>	5.70 ± 0.24 <sup>A</sup>	4.48 ± 0.13 <sup>A</sup>	4.14 ± 0.09 <sup>A</sup>	9.84 ± 0.38 <sup>CBFGH</sup>
	Oral	13.98 ± 1.29 <sup>d</sup>	10.44 ± 0.82 <sup>da</sup>	7.90 ± 0.55 <sup>da</sup>	6.80 ± 0.44 <sup>a</sup>	5.98 ± 0.48 <sup>ag</sup>	9.78 ± 0.66 <sup>dahi</sup>
48.4	IP	14.24 ± 0.84 <sup>C</sup>	5.60 ± 0.48 <sup>A</sup>	4.54 ± 0.46 <sup>A</sup>	3.36 ± 0.26 <sup>A</sup>	2.98 ± 0.22 <sup>A</sup>	8.02 ± 0.12 <sup>CADH</sup>
	Oral	14.44 ± 0.96 <sup>d</sup>	9.08 ± 0.43 <sup>da</sup>	6.50 ± 0.39 <sup>a</sup>	4.70 ± 0.21 <sup>a</sup>	4.04 ± 0.26 <sup>a</sup>	8.20 ± 0.40 <sup>dai</sup>
93.5	IP	14.10 ± 0.23 <sup>C</sup>	6.22 ± 0.28 <sup>A</sup>	5.26 ± 0.27 <sup>A</sup>	4.30 ± 0.32 <sup>A</sup>	3.72 ± 0.18 <sup>A</sup>	7.30 ± 0.29 <sup>AD</sup>
	Oral	19.44 ± 0.64 <sup>d</sup>	9.70 ± 0.58 <sup>da</sup>	6.74 ± 0.72 <sup>a</sup>	4.48 ± 0.37 <sup>ae</sup>	3.66 ± 0.21 <sup>ae</sup>	7.90 ± 0.36 <sup>dai</sup>
180.9	IP	13.16 ± 0.67 <sup>C</sup>	6.48 ± 0.70 <sup>A</sup>	4.74 ± 0.62 <sup>A</sup>	3.44 ± 0.29 <sup>A</sup>	2.88 ± 0.32 <sup>CAB</sup>	6.94 ± 0.20 <sup>AD</sup>
	Oral	14.78 ± 0.83 <sup>d</sup>	8.86 ± 0.45 <sup>da</sup>	7.12 ± 0.36 <sup>a</sup>	5.72 ± 0.42 <sup>a</sup>	4.56 ± 0.45 <sup>a</sup>	7.16 ± 0.22 <sup>ae</sup>
350	IP	12.66 ± 0.71 <sup>C</sup>	6.64 ± 0.73 <sup>A</sup>	4.66 ± 0.62 <sup>A</sup>	3.48 ± 0.43 <sup>A</sup>	3.00 ± 0.42 <sup>A</sup>	5.50 ± 0.60 <sup>ADE</sup>
	Oral	14.60 ± 0.86 <sup>d</sup>	10.18 ± 1.04 <sup>da</sup>	7.48 ± 0.22 <sup>a</sup>	5.52 ± 0.29 <sup>a</sup>	4.32 ± 0.17 <sup>a</sup>	5.14 ± 0.40 <sup>abef</sup>

**Table 1:** Effects of administration of five therapeutic doses of aqueous extracts of *Vernonia lasiopus* at different times on blood glucose levels in alloxan induced diabetic mice. Results are expressed as Means ± Standard Deviation for five mice per group. Means accompanied by similar upper-case letters and similar lower case letters in the same column are significantly different at  $p \leq 0.05$  by ANOVA and post ANOVA (Bonferroni-Holm) test. Means for IP administration:  $C_p < 0.05$  with respect to normal control;  $A_p < 0.05$  with respect to negative control;  $B_p < 0.05$  with respect to positive control;  $D_p < 0.05$  with respect to 25 mg/kg body weight;  $E_p < 0.05$  with respect to 48.4 mg/kg body weight;  $F_p < 0.05$  with respect to 93.5 mg/kg body weight;  $G_p < 0.05$  with respect to 180 mg/kg body weight;  $H_p < 0.05$  with respect to 350 mg/kg body weight. Means for Oral administration:  $d_p < 0.05$  with respect to normal control;  $a_p < 0.05$  with respect to negative control;  $b_p < 0.05$  with respect to positive control;  $e_p < 0.05$  with respect to 25 mg/kg body weight;  $f_p < 0.05$  with respect to 48.4 mg/kg body weight;  $g_p < 0.05$  with respect to 93.5 mg/kg body weight;  $h_p < 0.05$  with respect to 180 mg/kg body weight;  $i_p < 0.05$  with respect to 350 mg/kg body weight. Value followed by \* $p < 0.05$  is considered statistically significant when the mean of the oral group is compared to intraperitoneal group by T-test.

Pharmacokinetics of the blood glucose lowering effect of the extract of *V. lasiopus* for the first four hours is shown in Table 2. From the results pseudo-first-order rate constants for oral administration of aqueous extract of *V. lasiopus* at dosage of 25, 48.4, 93.5, 180.9 and 350 mg/kg were 0.2854, 0.3991, 0.381, 0.3652 and 0.3344, respectively and their calculated half-lives were 2.43, 1.74, 1.82, 1.90, and 2.07, respectively. All the other doses had lower half-lives than glibenclamide but 25 mg/kg showed higher half-life than the reference drug. Intraperitoneal administration of *V. lasiopus* extracts at 25, 48.4, 93.5, 180.9 and 350 mg/kg body weight showed Pseudo-first order rate constants at 0.445, 0.4152, 0.493, 0.5106 and 0.5998, respectively and

the half-lives associated with these constants were 1.56, 1.67, 1.41, 1.36 and 1.16, respectively. The half-lives of 93.5, 180.9 and 350 mg/kg body weight were lower compared to that of insulin while the other doses had higher half-lives than insulin. The orally administered extract of *Vernonia lasiopus* showed rate constant ranging from 0.2854 to 0.3991 per hour and half-life range of between 2.43 to 1.74 hours respectively. The range of the rate constant for the intraperitoneally administered extract of *Vernonia lasiopus* were from 0.4152 to 0.4152 per hour and their accompanying half-lives ranged from 1.67 to 1.16 hours, respectively. Insulin's rate constant was 0.4953 per hour while

glibenclamide was 0.3069 per hour and the half-life associated with them was 1.40 and 2.26 hours, respectively.



**Figure 1:** Percentage reduction in blood glucose levels at varying times after oral administration of the aqueous extracts of *Vernonia lasiopus* in alloxan induced diabetic male mice. Values are expressed as % means  $\pm$  SEM for five animals for each time point. <sup>d</sup> $p < 0.05$  when compared to normal control; <sup>a</sup> $p < 0.05$  when compared to negative control; <sup>b</sup> $p < 0.05$  when compared to positive control; <sup>c</sup> $p < 0.05$  when compared to 25 mg/kg body weight; <sup>f</sup> $p < 0.05$  when compared to 48.4 mg/kg body weight; <sup>s</sup> $p < 0.05$  when compared to 93.5 mg/kg body weight; <sup>h</sup> $p < 0.05$  when compared to 180 mg/kg body weight; <sup>i</sup> $p < 0.05$  when compared to 350 mg/kg body weight.

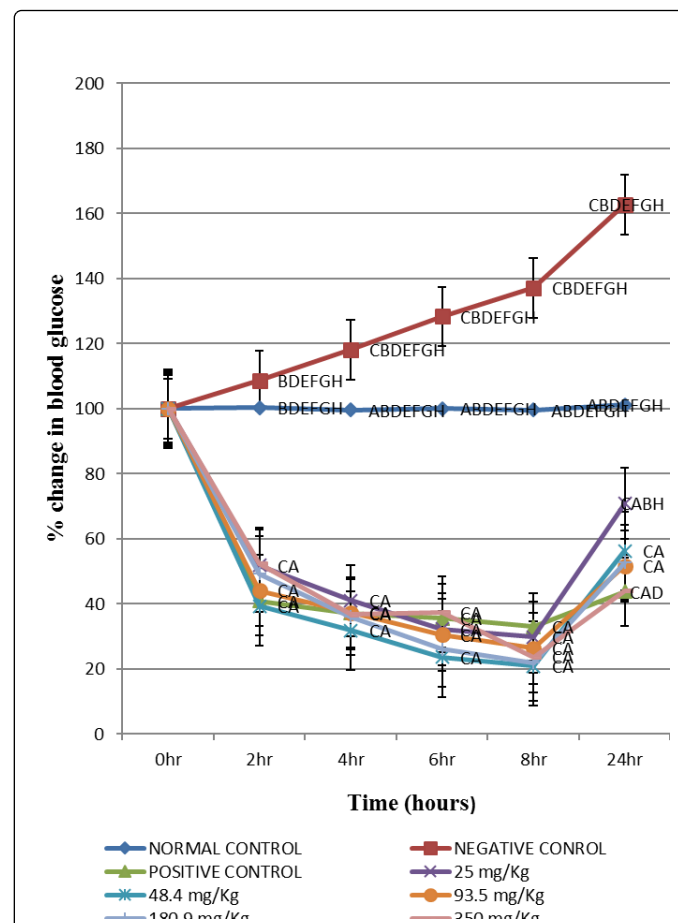
### Phytochemical screening results of extract of *Vernonia lasiopus*

The phytochemical screening results showed that the aqueous extract of *Vernonia lasiopus* contained Flavonoids, Terpenoids, Saponins, Alkaloids, and Tannins as shown in Table 3.

### Discussion

The leaves extract of *Vernonia lasiopus* exhibited a potent antidiabetic effect in alloxan-induced diabetic mice at all the doses administered (25, 48.4, 93.5, 180.9 and 350 milligrams per kilogram

body weight) without depending on the dose administered. The mechanism of plasma sugar decreasing effect could be explained by increase in glucose utilization by tissues such as liver cells, fat and muscles as a result of the activation of insulin receptors [16] or increased secretion of insulin as a result of stimulation of  $\beta$ -cells of the islet of Langerhans [17]. High insulin levels lead to a decrease in blood glucose levels [18] as a result of increased uptake of glucose by peripheral tissues which are due to mediation by GLUT-4. GUT-4 is a glucose transporter which depends on insulin [19].



**Figure 2:** Percentage reduction in blood glucose levels at varying times after intraperitoneal administration of the aqueous extracts of *Vernonia lasiopus* in alloxan induced diabetic male mice. Values are expressed as % means  $\pm$  SEM for five animals for each time point. <sup>C</sup> $p < 0.05$  when compared to normal control; <sup>A</sup> $p < 0.05$  when compared to negative control; <sup>B</sup> $p < 0.05$  when compared to positive control; <sup>D</sup> $p < 0.05$  when compared to 25 mg/kg body weight; <sup>E</sup> $p < 0.05$  when compared to 48.4 mg/kg body weight; <sup>F</sup> $p < 0.05$  when compared to 93.5 mg/kg body weight; <sup>G</sup> $p < 0.05$  when compared to 180 mg/kg body weight; <sup>H</sup> $p < 0.05$  when compared to 350 mg/kg body weight.

The *Vernonia lasiopus* aqueous extract decreased blood sugar in a manner not dependent on the dose administered both by intraperitoneal and oral route. The antihyperglycemic effect suggests that the *Vernonia lasiopus* extracts has hypoglycemic constituents. The blood sugar lowering without depending on the dose administered suggests uptake of glucose through an active transport that is saturable.

The greater rate of clearance of glucose from the plasma and short half-life observed on intraperitoneal administration as opposed to oral administration can be attributed to the high availability of active components to the systemic circulation. When the extract is administered orally the active constituent concentration in the systemic circulation is reduced the first-pass liver metabolism or had

limited absorption in gastrointestinal through the mucosal epithelial cells. The active constituents administered orally are absorbed by the mucosal epithelial cells where they are transported to the liver by hepatic portal vein. These constituents are metabolized in the liver after which reduced amounts of un-metabolized constituents are released into the systemic circulation [20].

Drug (dose)	Route	Rate constant (hour <sup>-1</sup> )	Half-life (hours)
Insulin	IP	0.4953	1.40
Glibenclamide	Oral	0.3069	2.26
Extract (mg/kg bw)			
25	IP	0.445	1.56
	Oral	0.2854	2.43
48.4	IP	0.4152	1.67
	Oral	0.3991	1.74
93.4	IP	0.493	1.41
	Oral	0.381	1.82
180.9	IP	0.5106	1.36
	Oral	0.3652	1.90
350	IP	0.5998	1.16
	Oral	0.3344	2.07

**Table 2:** Pharmacokinetics of the hypoglycemic activity for the first four hours of the five doses of the aqueous extracts of *V. lasiopus*. Results are expressed as Means of five mice for each time point; bw represents body weight.

Samples	Phytochemical Content (mg/g)				
	Total Phenols	Tannins	Flavonoids	Saponins	Alkaloids
<i>Vernonia lasiopus</i>	9.97 ± 0.23	2.56 ± 0.29	3.81 ± 0.05	53.73 ± 0.60	6.63 ± 0.14

**Table 3:** Quantitative screening of the phytochemicals in the medicinal plants extract. Quantities are expressed as Mean ± Standard Deviation (SD) of three determinations for each extract. The phytochemicals were expressed as mg per g of dry extract.

The antidiabetic effect of *Vernonia lasiopus* aqueous extracts could be attributed to the phytochemicals such as phenols, alkaloids, saponins, flavonoids and tannins which have been demonstrated to have antidiabetic effect [21].

The antidiabetic effect observed on administration of aqueous extract of *Vernonia lasiopus* could be due to flavonoids present in the extract. Glauce et al. [22], reported that a flavonoid polyhydroxylated flavonol stimulate glucose transport in adipose tissue as well as stimulating lipogenesis because it has insulinomimetic properties therefore lowering blood sugar [23]. Fractions of flavonoids from *Pterocarpus marsupii* have been demonstrated to cause regranulation of beta cells of pancreas. Flavonoid glycosides such as isostrictinin, pedunculagin, and strictinin are effective components of *Psidium*

*guajava*, which improve the sensitivity and are therefore used to manage of diabetes mellitus [24].

The aqueous leaf extracts of *Vernonia lasiopus* also contained tannins which have been demonstrated to have the hypoglycemic effect. Broadhurst et al. [25] have demonstrated that tannin epigallocatechin-3-gallate shows antidiabetic activity. The extract of *Vernonia lasiopus* also contained saponins. Saponins have been shown to have antihyperglycemic activity. For instance, ginseng has saponins that have been shown to decrease blood glucose level diabetic mice [26].

The aqueous leaf extracts of *Lippia javanica* have been demonstrated to have a hypoglycemic activity which is attributed to the alkaloids alkaloids present. Alkaloid fractions from *C. decidua* have also demonstrated antidiabetic activity in mice [27]. Alkaloids such as tetrandine and Berberine have been shown to have antioxidant activity which is responsible for biological activities shown by the plant among them antidiabetic effect. The herb *Ephedra distachya* contains alkaloid l-ephedrine which have demonstrated antidiabetic effect in mice by regenerating and restoring atrophied islets of pancreases hence inducing insulin production [1,23].

## Conclusion

The study has shown that aqueous leaves extracts from *Vernonia lasiopus* had antidiabetic activity which may be due to the phytochemicals present. Intraperitoneal route of drug administration was found to be more effective than the oral route from rate of glucose

clearance from the systemic circulation the associated half-life. This study recommends the use of *Vernonia lasiopus* in management of diabetes mellitus.

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