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Hypoglycemic and Hepatorenal Effect of *Ocimium gratissimium* in Alloxan Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author BH designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author GTD managed the analyses of the study. Author IG managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Diabetes Mellitus is a disease of public health concern which is caused by pancreatic defect in insulin secretion or failure of the receptor cells to effectively utilize secreted insulin. Diabetes account for 2-3% death in the poorest countries hence the need for alternative control measure. This stud evaluated the hypoglycemic and hepatorenal effect of *Ocimium gratissimium* and glibenclamide in alloxan induced diabetic rats. Twenty- four rats were randomly divided into 6 groups of 4 animals in each group (1,2,3,4,5 & 6), groups 2,3,4,5 & 6 were induced diabetes intraperitoneally with 150 mg\kg alloxan (Sigma Ltd), diabetes was confirmed by fasting blood glucose of >10.0mmol/L. Groups 3,4,5 & 6 were subsequently treated with 400 mg/kg of extract, 5mg glibenclamide, 800 mg/kg of extract, 400 mg/kg extract combined with 5mg glibenclamide respectively. Blood glucose, hepatic function variables (Aspartate aminotransferase (AST), Alanine aminotransferase(ALT), Total bilirubin (TB) and renal parameters Sodium (Na^+), Potassium (K^+), Urea were analyzed. The result shows an increase in glucose, hepatic and renal parameters in diabetic induced groups which was significantly reduced in a dose dependent manner in the

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diabetic treated groups, the high dose of the extract (800mg/kg) was more effective in blood glucose reduction than the standard antidiabetic drug, (5mg glibenclamide). However, 5mg glibenclamide was found to be more effective in blood glucose reduction than the low dose (400mg/kg) extract, the combination of 5mg glibenclamide and 400mg/kg was found to be more effective in blood glucose reduction than the low dose extract. A significant increase was observed in the Total bilirubin and urea parameters of the high dose (800mg/kg) of the extract treated groups and in the combined group (400 mg/kg+5 mg glibenclamide). When compared to the low dose extract group(400mg/kg). Low dose *ocimium gratissimium* potentiates 5mg glibenclamide in blood glucose reduction. *Ocimium gratissimium* and glibenclamide decreased blood glucose and ameliorates alloxan induced hepatic and renal damage. The use of the high dose of the extract and the use of the combination of the drug (5mg glibenclamide) and the low dose of the extract in diabetes management may be detrimental to the liver and kidney according to this study.

Keywords: Diabetes; Ocimium gratissimium; glibenclamide; hepatic; renal.

1. INTRODUCTION

Diabetes is an important chronic metabolic disorder of public health concern. It occurs as a result of pancreatic defect in insulin secretion or failure of the receptor cells to effectively utilize secreted insulin or both resulting in hyperglycemia which can lead to damage to the vascular tissues in the eyes, heart, nerves, or kidney causing retinopathy, cardiopathy neuropathy or nephropathy [1].

Diabetes is caused by absolute or relative insulin deficiency. It has been defined by the World Health Organization (WHO) on the basis of laboratory findings as fasting plasma glucose concentration of 7.0mmol/1 or more on more than one occasion or once in the presence of diabetes symptoms and plasma glucose level of 11.1mmol/L or more after ingestion of equivalent of 75g anhydrous glucose.

The kidney and liver play significant role in glucose homeostasis. The liver acts to maintain normal glucose level during fasting and post prandial period [2].

Furthermore, hyperglycemia which is the hallmark of diabetes leads to glucosuria. When the blood glucose rises to relatively high level, the kidney exerts a regulatory effect. Glucose is continuously filtered by the glomeruli but is ordinarily returned completely to the blood by the re-absorptive system of the renal tubule. When the blood glucose level is elevated, the glomerular filtrate may contain more glucose than can be reabsorbed. The excess glucose passes to the urine producing glycosuria. This can result in nephrotoxicity [3].

Diabetes is a major cause of morbidity and mortality in both developing and developed countries [4]. It is expected that the incidence will be rising rapidly with sub-saharan Africa experiencing the largest increase between 2013 and 2035. In Africa, Nigeria has the highest number of people with diabetes about 62% of estimated value [5].

Diabetes have no known cure. Consequently, herbal remedies providing a new promising approach has to be explored. The use of natural product or synthetic agent alone or in combination to prevent diabetes in humans is promising [6]. About 40-60% of diabetic patient in Nigeria use non-conventional treatment for diabetes, of which 23% of these use botanicals alone. WHO (1989) in its general assembly authenticated this approach [7].

Ocimium gratissimium is one of the herbs used in the treatment of diabetes. The use of natural remedies for diabetes is also strengthened due to the belief that herbs can provide some benefit over and above allopathic medicines and allows users to feel that they have control of their choice of medications [8]. Some medicinal plants may produce adverse long-term effects such as hepatoxicity and nephrotoxicity [9]. This study investigated the hypoglycemic and hepatorenal effect of *Ocimium gratissimium* extract on alloxan-induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Preparation of the Extract

Fresh leaves of the plant were properly washed with deionized water to remove debris. The leaves were dried under room temperature and pulverized using warring blender. The extraction

was done using Batch Extraction Method with methanol as extracting solvent. A weighed portion of the pulverized sample (2kg) was soaked in 1000ml of absolute methanol (BDH chemicals) for 72hrs. The supernatant was decanted and filtered into 1000ml conical flask through Whatman filter paper. The extracts were concentrated using rotary evaporator set at 60◦C.

The phytochemicals of interest were determined using UV visible analysis with the wavelength range of 200-1100nm. At each wavelength its adsorption was compared with UV developed standard for phytochemicals to determine the phytochemicals present. 100 g of the dried sample was weighed and used for quantitative analysis.

2.2 Experimental Animals

Twenty-Four male wistar rats weighing 120-150 g were purchased from animal farm of the pharmacy Department of the University of Port Harcourt, Nigeria. The rats were housed in animal cages in a well-ventilated experiment room. The rats were allowed to acclimatize for 14 days prior to the commencement of treatment in a 12 hourly light and dark cycle. They were allowed access to standard feed (finisher) manufactured by Top feeds Nigeria Limited and water ad *Libitum*. Handling of animals was in accordance with National Institute of Health (NIH).

2.3 Preparation of Drug, Glibenclamide (5 mg)

The standard drug glibenbclamide used for this study was purchased from a registered pharmacy in Port Harcourt. 200 mg of the glibenclamide was dissolved 40 ml of distilled water and administered to appropriate animals through oral route.

2.4 Preparation of Alloxan and Induction of Diabetes

Diabetes was induced according to a method adopted by [10]. One (l) gram of alloxan, a product of sigma chemicals USA was dissolved in 10mls of distilled water. Prior to commencement of induction of diabetes, all the animals were weighed. 150mg/kg of alloxan was injected intraperitonially to appropriate groups of animals lo induce diabetes. Diabetes was confirmed according to [11] 3days after alloxan administration with one touch glucometer (life scan) by a reading of fasting blood sugar (>10mmol/l). The rats were randomly assigned into treatment groupings and appropriate treatments were commenced.

2.5 Experimental Design

Twenty- four male albino rats weighing 120-150 g were grouped into six groups; 2,3,4,5, & 6 were induced with 150mg/kg alloxan, groups 3,4,5&6 received various treatment dosages for four week as shown.

2.6 Diabetic Rats

The blood glucose of experimental animals was determined on day 7, 14 and 21 of the experimental periods. It was observed that the fasting blood glucose of the negative control group maintain a normal blood group level throughout the experimental period while the fasting blood glucose of the positive control group maintained high fasting blood glucose throughout the experimental periods with a blood level >10.0mmol/L. values > 10.0mmol was considered diabetic.

2.7 Statistical Analysis

The statistical analyses were expressed as mean ± SEM for hepatic and renal parameters. The comparison of data for glucose, hepatic and renal parameters from test and control groups

Table 1. Dosages, administration and duration of treatment on alloxan induced

Groups	Treatments	Dosage/Administration
Group 1	Normal feed + water	
Group 2	Diabetic Group	Diabetes + Normal feed & water
Group 3	Diabetes + low dose Extract	400 mg/kg/4weeks
Group 4	Diabetes+ Drug(5mg glibenclamide)	200 mg/kg/4weeks
Group 5	Diabetes + Extract High Dose	800 mg/kg/4weeks
Group 6	Diabetes + Extract + Drug (5mg glibenclamide)	400 mg/kg + 200mg/kg/4weeks

Table 2. Blood Glucose pattern before, during and after treatment with alloxan induced diabetic rats expressed in mmol/L

Groups	Treatments	Baseline glucose level	Treatment day 7 glucose	Treatment phase day 14	Treatment phase day 21
Group 1	Normal feeds + water	5.40	5.03	4.85	5.23
Group 2	Diabetic + feeds + water	5.55	14.56	15.53	16.20
Group 3	Diabetes + 400mg of extract	5.75	12.25	10.65	8.45
Group 4	Diabetes + Drug (glibenclamide)	5.33	9.75	7.65	5.22
Group 5	Diabetes + 800mg of extract	5.28	8.25	8.04	4.86
Group 6	Diabetes +400mg of *Ociimium gratissimium*+5mg glibenclamide	5.30	8.27	6.00	4.85

were analyzed using one-way analysis of variance (ANOVA) at $p > 0.05$ level of significance were considered significant for hepatic and renal parameters. It was determined with SPSS version 23 IBM.

3. RESULTS

3.1 Result of Phytochemicals Analysis of *Ocimium gratissimium*

This research wok evaluated the hypoglycemic and hepato-renal effect of *Ocimium gratissimium* in alloxan induced diabetic rats. The analysis of the ethanol extract of *Ocimium gratissimium* showed the presence of Flavonoid, Tannins, Phenols and Alkaloids. Phenols and Alkaloids with the concentration of 1.96 ± 0.12, 1.02 ± 0.02, 2.71 ± 0.21, 2.62 ± 0.02 respectively in 100g dry weight (Table 3).

3.2 Result of Multiple Comparison of Mean Glucose Level by Duration of Treatment

Table 4 summarized the comparison of mean glucose levels of groups by duration of treatment. From the comparison, a significant increase was observed in the blood glucose of experimental animal on day 7[14.56±0.04mmol/L], day 14[15.53±0.06mmol/L], day 21[16.20±0.0mmol/L] of diabetic control group when compared to their baseline glucose [5.03±0.02mmol/L] [4.85±0.03mmol/L] [5.23±0.02mmol/L], This increase was significantly reduced in various treatment groups; 3,4,5&6. At the end of the experiment period, there was no significant difference in the blood glucose of day 21 negative control [5.23±0.02mmol/L] and their baseline glucose [5.4±0.02mmol/L] indicating that at the end of the increase in blood glucose resulting from diabetes reduction has been normalized.

A significant increase was observed in the blood glucose of positive control on day 14[15.53±0.06mmol/L], when compared to day 7[14.56±0.06mmol/L], also the blood glucose of day 21 [16.20±0.07mmol/L] increases significantly when compared to day 7 [14.56±0.06mmol/L] confirming hyperglycemia in uncontrolled diabetes. On the contrary the blood glucose continuous increase following duration in diabetic control group was significantly reduced in a dose dependent manner in the groups that received various treatment dosages (group 3,4,5&6) this shows that blood glucose reduction dependent on dosage and duration this is summarize in Table 4.

3.3 Result of Multiple Comparison of Mean Glucose Levels of Various Treatment Dosages with Control Groups

Table 5 summarized the multiple comparison of mean glucose of various treatment dosages with control groups, A significant increase was observed in blood glucose of the positive control

Table 3. Qualitative and quantitative screening for phytochemical components in sample C_1 (Encoded C_1)

	Components (100 g dry weight)	Sample C_1 (MEAN±STD) (mg)
1	Flavonoid	+1.96±0.12
2	Eugenol	-
3	Saponin	-
4	Tannin	+1.02±0.02
5	Phenol	++2.71±0,21
6	Alkaloid	++2.62±0.02

Key: ++ Absolutely detected + Moderately detected - Not detected

group 2 on day 7 [14.56±0.04, 15.53±0.06, 16.20±0.07mmol/L] positive control when compared to the negative control group 1, day 7 [5.03±0.02mmol/L], day 14 [4.85±0.03mmol/L], day 21 [5.23±0.02mmol/L] this was followed by a gradual dose dependent reduction in various treatment group; 3,4,5&6, such that at the end of the experimental period it was observed that the blood glucose has been normalize in diabetes treated in group 4,5&6 that is (group treated with 5mg/kg glibenclamide, 800mg/kg of extract and the combination of 5mg glibenclamide with 400 mg/kg of extract.

A significant dose dependent reduction has observed in blood glucose of diabetes treated group 6; 400mg/kg combined 5 mg glibenclamide [4.80±0.01mmol/L] when compared to diabetes low dose of extract; 400 mg/kg [8.45±0.01mmol/L].

3.4 Result of Multiple Comparisons of Mean Values of Some Liver Variables of Control Group and test Groups

Table 6 shows the multiple comparisons of mean hepatic values of some liver variables of control groups and other groups. There was significant increase in the mean hepatic parameters of positive control, AST [107±2.5mmol/L], ALT [92.25±3.15mmol/L], TB[36.08±0.55mmol/L], when compared to the negative control, AST (49.50±2.2mmol/L)), ALT (49.20±4.18mmol/L), TB (30.43±0,68). Comparison of diabetic treated groups; 3, 4, 5&6. There was no significant difference in their mean hepatic parameters except in diabetic treated with 5mg glibenclamide [24.60±0.035mmol/L] and diabetic treated with (800mg/kg) of extract [29.9 ±0.34mmol/L] diabetic treated with 400 mg extract with 5mg glibenclamide [30.00 ± 0.80mmol/L], where there was a significant reduction in total bilirubin when compared to the negative control 1 [30.43 ± 0.63mmol/L]. There was a significant reduction in all the hepatic parameters of diabetic treated groups; 3,4,5&6 when compared to the positive control. Comparison of diabetic treated with 400mg/kg of extract, group 3 with diabetic with 5mg glibenclamide, group 4 and diabetic treated with 800mg/kg of extract, group 5 and diabetic treated with 400mg of extract combined with 5mg glibenclamide, group 6 shows no significant difference in all the hepatic parameters except for total bilirubin, which shows a significant increase was in diabetic treated with high dose (800 mg/kg) [29.9 ± 0.30mmol/L] and diabetic treated with combination of 400mg of extract with 5mg glibenclamide (3000+0.80mm0l/L) when compared to diabetic treated with low dose, group 3[24.96 ± 0.34mmol/L]. Comparison of diabetic treated with 5mg glibenclamide, group 4 with diabetic treated with high dose (800mg/kg) of extract, group 5 shows no significant difference in the mean hepatic parameters except for total bilirubin, where an increase was observed in diabetic treated with high dose 800mg/kg[29.9 ± 0.34mmol/L] when compared to diabetic treated with standard drug group 4 [24.60 ± 0.34mmol/L].

3.5 Result of Multiple Comparison of Mean Values of Some Renal Variables of Control Group and Test Groups

Table 7 shows the multiple comparison of some mean renal variables of control groups with other groups, there was a significant increase in all the renal parameters of the positive control Na^+[147.75±0.8mmol/L],urea[8.10±0.47mmol/L], k^+[6.55 ± 0.12mmol/L] compared to the negative control group Na^+ [150.50±1.38mmol/lL], urea [6.53±0.07mmol/L], k^+[3.75 ± 0.025mmol/L] except for Na^+ where there was no significant change.

Table 4. Multiple comparison of mean glucose levels of groups by duration of treatment (Expressed as mean ± SEM)

	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Baseline glucose/mmol/L	5.40 ± 0.12	5.55 ± 0.04	5.75 ± 0.04	5.33 ± 0.05	5.28 ± 0.05	5.30+0.01
Treatment day 7	5.03 ± 0.02	14.56 ± 0.04	12.25 ± 0.09	9.75 ± 0.02	8.25 ± 0.02	8.27+0.02
Treatment day 14	4.85 ± 0.03	15.53 ± 0.06	10.65 ± 0.08	7.65 ± 0.01	6.04 ± 0.01	6.00+0.01
Treatment day 21	5.23 ± 0.02	16.20 ± 0.07	8.45 ± 0.02	5.22 ± 0.02	4.86 ± 0.01	4.80+0.01
F-values	18.35	21.73	75.38	49.615	22.23	22.23
p-values	<0. 0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Tukey's Multiple Comparison Test	Summary	Summary	Summary	Summary	Summary	
Baseline vs Day 7	**	***	***	***	***	***
Baseline vs Day 14	***	***	***	***	***	***
Baseline vs Day 21	Ns	***	***	***	***	***
Day7 vs Day 14	Ns	***	***	***	***	***
Day 7vs Day 21	Ns	***	***	***	***	***
Day 14 vs Day 21	**	***	***	***	***	***

*ANOVA followed by tukey's multiple comparism; Ns - No significant difference; *- Significant difference; ** - Moderate Significant difference; *** - High Significant difference; Group 1 - Negative control; Group 2 - Positive control – Diabetic Ad Libitum; Group 3 - Diabetic treated with low dose (400mg/kg) Ocimium gratissimium extract; Group 4 - Diabetic + (5 mg glibenclamide); Group 5 - Diabetic + high dose (800mg) Ocimium gratissimium; Group 6 - Diabetes + 400mg Ocimium gratissimium + 5 mg glibenclamid*

Table 5. Multiple comparison of mean glucose of various treatment dosage with control

Group	Baseline glucose level/mmol\l	Treatment day 7	Treatment day 14	Treatment day 21
Group 1	5.4± 0.12	5.03 ±0.02	4.85±0.03	5.23±0.02
Group 2	5.55 ±0.04	14.56±0.04	15.53±0.06	16.20±0.07
Group 3	5.75 ±0.04	12.25±0.09	10.65±0.08	8.45±0.02
Group 4	5.33 ±0.05	9.75±0.02	7.65±0.01	5.22±0.02
Group 5	5.28±0,05	8.25±0.02	6/04±0.1	4.86±0.01
Group 6	5.30±0.01	8.27±0.02	6.00±0.01	4.80±0.01
F-values	1.835	91.39	55.46	35.43
P values	0.1687	<0.0001	<0.0001	<0.0001
Turkey's multiple comparison Test	Summary	Summary	Summary	Summary
Group1 vs group 2	Ns	***	***	***
Group vs group 3	Ns	***	***	***
Group 1 vs group 4	Ns	***	***	Ns
Group 2 vs group 3	Ns	***	***	***
Group 2 vs group 4	Ns	***	***	***
Group 2 vs group 5	Ns	***	***	***
Group 2 vs group 6	Ns	***	***	***
Group 3 vs group 4	Ns	***	***	**
Group 3 vs group 5	Ns	***	***	**
Group 3 vs group 6	Ns	***	***	**
Group 4 vs group 5	Ns	***	***	Ns
Group 4 vs group 6	Ns	***	***	*

*ANOVA followed by tukey's multiple comparion; Ns - No significant difference; * - Significant difference; ** - Moderate Significant difference; *** - High Significant difference*

Table 6. Multiple comparison of Mean values of some liver variables of control group and other groups

Groups	AST (U/L)	ALT (U/L)	TB (mmol/L)
Group 1	49.50 ± 2.2	49.2 ± 4.18	30.43 ± 0.68
Group 2	107.50± 2.5	92.25± 3.15	36.08± 0.55
Group 3	42.50± 2.5	27.75±2.17	24.96±0.34
Group 4	42.75± 1.83	30.5±3.12	24.60± 0.35
Group 5	49± 1.93	32± 1.98	29.95± 0.34
Group 6	51±0.33	33±0.90	30.00±0.80
F-values	51.89	20.12	20.72
P-values	< 0.0001	< 0.0001	< 0.0001
Tukey's Multiple Comparison Test	Summary	Summary	Summary
Group 1 vs Group 2	***	**	*
Group 1 vs Group 3	Ns	Ns	*
Group 1 vs Group 4	Ns	Ns	**
Group 1 vs Group 5	Ns	Ns	Ns
Group1 vs Group 6	Ns	Ns	*
Group 2 vs Group 3	***	***	***
Group 2 vs Group 4	***	***	***
Group 2 vs Group 5	***	***	**
Group 2 vs Group 6	***	***	**
Group 3 vs Group 4	Ns	Ns	Ns
Group 3 vs Group 5	Ns	Ns	*
Group3 vs Group 6	Ns	Ns	*
Group 4 vs Group 5	Ns	Ns	*
Group 4 vs Group6	Ns	Ns	*

*ANOVA, followed by Tukey's Multiple Comparison; Ns = No significant difference; * = Significant difference; ** = Moderate Significant difference; *** = High Significant difference; AST = Aspartate aminotransferase, ALT = Alanine aminotransferase, TB = Total Bilirubin*

Table 7. Multiple comparison of Mean values of some renal variables of control group and test groups

Groups	Na^+ (mmol/L)	UREA (mmol/L)	K^+ (mmol/L)
Group 1	150.50 ± 1.38	6.53 ± 0.07	3.75 ± 0.25
Group 2	147.75 ± 0.87	8.10 ± 0.4	6.55 ± 0.12
Group 3	151.50 ± 0.73	4.28± 0.19	5.1 ±0.17
Group 4	149.25 ± 0.63	6.20 ± 0.13	4.4 ±0.18
Group 5	146.75 ± 0.73	6.43 ± 0.06	3.80 ± 0.29
Group 6	147.00±0.47	6.45±0.05	3.81±0.66
F-values	1.546	1.33	8.731
P-values	0.2029	<0.0001	<0.0001
Tukey's Multiple Comparison Test	Summary	Summary	Summary
Group 1 vs Group 2	Ns	*	**
Group 1 vs Group 3	Ns	**	Ns
Group 1 vs Group 4	Ns	Ns	Ns
Group 1 vs Group 5	Ns	Ns	Ns
Group 1 vs Group 6	Ns	Ns	Ns
Group 2 vs Group 3	Ns	***	Ns
Group 2 vs Group 4	Ns	*	*
Group 2 vs Group 5	Ns	*	**
Group 2 vs Group 6	Ns	*	**
Group 3 vs Group 4	Ns	**	Ns
Group 3 vs Group 5	Ns	**	Ns
Group 3 vs Group 6	Ns	**	Ns
Group 4 vs Group 5	Ns	Ns	Ns
Group 4 vs Group 6	Ns	Ns	Ns

*ANOVA, followed by Turkey's multiple comparisons; Ns = No significant difference; * = Significant difference; ** = Moderate Significant difference; *** = High Significant difference; Na^+ = Sodium; K^+ = Potassium*

Comparison of the negative control with diabetic treated groups 3,4,5&6 shows no significant difference except in diabetic treated with low dose group 3, where there was significant reduction in urea [4.28 ± 0.19mmol/L] when compared to the negative control, [6.53 ± 0.07mmol/L]. Comparison of the positive control with diabetic treated groups, 3,4,5&6 shows a significant reduction in all the mean renal parameters except for Na^+ where there was no significant change.

Comparison of diabetic treated with low dose of 400mg/kg of extract, group 3 with diabetic treated with standard drug, glibenclamide group 4 and diabetic treated with high dose (800mg/kg) of the extract group 5 and diabetic treated , there was no significant difference in all the renal parameters, except urea, which shows a significant increase in diabetic group 4, that is diabetic treated with standard drug, glibencladmide [6.20 ± 0.13mmol/L] and diabetic treated with high dose (800mg/kg), group 5 [6.43± 0.06mmol] when compared to group 3 [4.28 ± 0.19mmol/L].

Comparison of diabetic treated with standard drug 5mg glibenclamide group 4 with diabetic treated with high dose (800mg\kg) of the extract, group 5 and diabetic treated with combination of 400mg of extract with 5mg glibenclamide, group 6, shows no significant difference in all their renal parameters. This was summarized in Table 4, 5.

4. DISCUSSION

Diabetes have no known cure; herbal products or synthetic product is used in the management of diabetes. Over production of reactive oxygen species (ROS) reinforces oxidative stress common to tissue injury mechanism associated with common clinical diseases such as diabetes, cancer etc. [12] majority of hepatotoxic chemicals damage the liver, subsequently the kidney through lipid peroxidation and other oxidative forms. Management of diabetes with synthetic drugs produces adverse effect on the major organ involved in glucose metabolism such as liver and kidney hence the need for an alternative control measure, *Ocimium gratissimium* is one of the herbs used in the management of diabetes. The result of the phytochemical analysis of the ethanol extract of *Ocimium gratissimium* of this study revealed the presence of Flavonoid, Tannins, Phenols and Alkaloids. Phenols and

Alkaloids with the concentration in mg of 1.96 ± 0.12, 1.02 ± 0.02, 2.71 ± 0.21, 2.62 ± 0.02 respectively in 100g dry weight. Phenolic and flavonoids compound known to be anti-lipid peroxidant and free radical scavengers [13].

Alloxan is a cytotoxic agent used to induce diabetes in this study, administration of alloxan resulted to a significant increase in blood glucose of animals at $p<0.0001$ in the diabetic induced groups, this is in agreement with the findings of [14]. Treatment of the experimental animals in the diabetic groups resulted to a dose dependent decrease in their blood glucose level, this is in agreement with findings of [15]. The multiple comparison of mean glucose level of groups by duration of treatment reflects that the negative control group maintained normal blood glucose level throughout the experimental periods (day 7,14 and 21). On the contrary the positive control (diabetic group) a continuous blood glucose increases as the period increases. A significant increase was observed in the blood glucose of positive control of day 14(15.53±0.06 mmol\L) when compared to day7(14.56±0.06mmol\L),.also a significant increase was observed in the blood glucose level of day 21(16.20±0.07mmol\L) when compared to day 14(15.53±0.06mmol\L) confirming hyperglycemia in uncontrolled diabetes, this increase, gradually reduces to normal in diabetic treated groups in a dose dependent manner at the end of the experimental period in diabetic treated with 5mg glibenclamide, diabetic treated with high dose9800mg\kg), diabetic treated with 5 mg glibenclamide combined with low dose extract(400mg\kg) .This indicates that glucose reduction is dependent on dosage and duration.

Multiple comparison of various treatment dosages with control groups reflects that the high dose of(800mg\kg) of *Ocimium gratissimium* extract was more effective in blood glucose reduction than the standard antidiabetic drug 5mg glibenclamide, however the standard antidiabetic drug 5mg glibenclamide was found to be more effective in blood glucose reduction than the low dose(400mg\kg) of *Ocimium gratissimium* extract. The diabetic treated with combination of 5mg glibenclamide and low dose *Ocimium gratissimium* caused a significant reduction in blood glucose level at $p<0.0001$ when compared to diabetic treated with low dose extract(400mg\kg) administered as a single dose indicating that the low dose *Ocimium gratissimium* potentiates glibenclamide in blood glucose reduction.

The detoxification function of the liver places the hepatocytes at the risk of destruction by cytotoxic drugs in the course of performing their duty. The classic view on the pathogenesis of drug-induced liver injury is that the so-called parent compounds are made hepatotoxic by metabolism, mainly by cytochromes P-450 [16]. Alloxan administration also resulted to hepatic damage. The liver enzymes Aspartate aminotransferase (AST) and Alanine Aminotransferase (ALT) which are intracellularly located, an injury to the liver releases them to the extracellular fluid(ECF) increasing their activity in serum. In addition, bilirubin is increased as a result of degenerating red blood cells as observed in diabetic control group of this study. Treatment of the diabetic control group with *Ocimium gratissimium* and glibenclamide resulted to a dose dependent decrease in these hepatic parameters this in agreement with the findings of [17].

Multiple comparison mean renal variables of control groups and other groups reflects an altered Renal Parameters increasing their level in serum except Na, as observed in diabetic control group of this study. Treatment of the diabetic control group with *Ocimium gratissimium* and glibenclamide resulted to a dose dependent decrease in the increased renal variables. This resulted to the restoration of hepatic renal parameters altered as a result of alloxan administration. A restoration of oxidant/anti-oxidant balance is further reflected in the ameliorated hepatic as shown in this study.

The probable mechanism of action of *Ocimium gratissimium* in hypoglycemic and ameliorating effect on alloxan induced hepatic and renal damage may be linked to the anti-oxidant phytochemicals of the plant.

The statistical increase in total bilirubin and urea level of the animal in diabetes treated with high dose (800mg/kg) of *Ocimium gratissimium* and those of in the combine group (diabetes treated with low dose; 400mg/kg of extract +5mg glibenclamide is a pointer to probable damage to the liver and kidney by the used of high dose of the extract and in combination with the drug in the management of diabetes.

5. CONCLUSION

This study reveals that both *Ocimium gratissimium* and glibenclamide have strong hypoglycemic as well as ameliorating effect on

alloxan induced hepatic and renal damage. The observed therapeutic effect on diabetes and alloxan induced hepatic and renal damage is dependent on duration and dosage, but may not be safe at high doses and when use in combination. 400mg *Ocimium gratissimium* potentiates 5mg glibenclamide in blood glucose reduction. The therapeutic property of *Ocimium gratissimium* may be linked to the phytochemical constituent of the plant with antioxidant property.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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