



**COMPARATIVE ASSESSMENT OF *OCCIMUM GRATISSIMUM* AND *CYMBOPOGAN CITRATUM* MIXTURE ON SOME BIOLOGICAL PARAMETERS IN DIABETIC WISTAR RATS**

<sup>1</sup>Durodola S. D., <sup>1\*</sup>Olorunfemi O. J., <sup>1</sup>Azibalua A. A., <sup>1</sup>Dum-Awara B. L., <sup>2</sup>Kiridi Emily G. E. and <sup>1</sup>Solomon M. Uvoh

<sup>1</sup>Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba Nigeria.

<sup>2</sup>Department of Human Physiology, Faculty of Basic Medical Sciences, Niger Delta University, Wilberforce Island, Amassoma, Bayelsa State, Nigeria.

\*Corresponding Author: Dr. Olorunfemi O. J.

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba Nigeria.

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**ABSTRACT**

The leave extracts *cymbopogan citratum* and *occimum gratissimum* are ayurvedic medicinal plants used in Nigeria to treat several ailments. Previous studies indicated that these plants possess hypolipidemic and antioxidant potential, functions which are preventive. The present study was aimed at investigating the therapeutic effects of these plants on already established diabetes in rats. Three different treatments (400 mg/kg, given for four weeks) used in this study effectively demonstrated significant ( $p < 0.05$ ) homeostatic re-alignment on disrupted lipid parameters caused by diabetes in hypercholesterolemic rats. Further, all three treatments also improved significantly ( $p < 0.05$ ) the electrolyte profile status. Overall, combination (mixture of the two plant extracts had the maximum effect on hypercholesterolemic rats followed by individual extracts when administered singly that may be due to varying concentrations of the different classes of phytochemicals. In conclusion, the mixture, synergistically, produced a far reaching positive influence on general body homeostasis taking into consideration, glucose, lipids, electrolytes and urea and creatinine balance.

**KEYWORDS:** *cymbopogan citratum*, *occimum gratissimum*, hypolipidemic, diabetes, rats.

**1. INTRODUCTION**

*Ocimum gratissimum*, also known as clove basil, African basil, (Nadkarni, 1999) and in Hawaii as wild basil, (Effraim et al, 2003] is a species of *Ocimum*. It is native to Africa, Madagascar, southern Asia, and the Bismarck Archipelago, and naturalized in Polynesia, Hawaii, Mexico, Panama, West Indies, Brazil, and Bolivia. (Rabelo et al, 2003). *gratissimum* is a herbaceous plant which belongs to the Labiatae family. The plant is indigenous to tropical areas especially India and it is also in West Africa. In Nigeria, it is found in the Savannah and coastal areas. The plant is commonly used in folk medicine to treat different diseases such as upper respiratory tract infections, diarrhoea, headache, diseases of the eye, skin diseases, pneumonia, cough, fever and conjunctivitis [Adebolu et al, 2005]. The infusion of *O. gratissimum* leaves is used as pulmonary antiseptic, antitussivum and antispasmodicum [Ngassoum et al, 2003].

Diabetes is a complex condition with a variety of causes and pathophysiology. The current single target approach

has not provided ideal clinical outcomes for the treatment of the disease and its complications. Herbal medicine has been used for the management of various diseases such as diabetes over centuries. Many diabetic patients are known to use herbal medicines with antidiabetic properties in addition to their mainstream treatments, which may present both a benefit as well as potential risk to effective management of their disease. Many common herbs and spices are claimed to have blood sugar lowering properties that make them useful for people with or at high risk of type 2 diabetes. Despite this potential, antidiabetic plants remain grossly understudied and under-utilized as a source of novel medication, particularly within the developed countries [Ngugi et al, 2012].

**2. MATERIALS AND METHODS**

**2.1 Experimental Animals**

Thirty (30) male Wistar rats with weights between 140 and 150 g were obtained from the Experimental Animal Farm of the University of Port Harcourt, Nigeria. The Wistar rats were housed in animal cages in a well-

ventilated experimental room. The rats were allowed to acclimatize for a period of 14 days before the commencement of treatments. The rats had free access to standard rat chow and clean water ad libitum. Handling of animals was in accordance with relevant institutional

and ethical guidelines as approved for scientific study. The rats were randomly sorted into five groups called treatment groupings and appropriate treatments were commenced subsequently.

### Experimental Design and Animal Groupings

	Grouping	Treatment
1	Negative control	(saline-treated)
2	Positive control	Diabetic (100mg/kg Streptozotocin)
3	Diabetes + Extract 1	<i>Ocimum gratissimum</i> (400mg/kg)
4	Diabetes + Extract 2	<i>Cymbopogon .citratus</i> (400mg/kg)
5	Diabetes + extracts 1 & extract 2	<i>O. Gratissimum</i> + <i>C. Citratus</i> (400mg/kg each)
6	Diabetes + insulin	Insulin (5-7U/day)

### 2.2. Collection of Plant Materials and Extraction

Stalks of *C. citratus* and *O. Gratissimum* were collected in the rural area of Akure, Ondo State and the sample voucher (045309) was deposited in the Herbarium, Faculty of Science, and University of Port Harcourt.

### Plants Extraction

#### *Cymbopogon citratus*

The collected *C. citratus* was cleaned and isolated into leaves, stems, and roots. They were separately oven-dried at 65°C and coarsely ground. The powdered materials of *C. citratus* (100 g) were extracted with 1000 mL of 70% methanol for 3 days with occasional shaking. A mixture of each part of the plant was filtered through Whatman qualitative grade 1 filter paper and this procedure was repeated 3 times. The extracts were then evaporated on a rotary evaporator (Gucci, Germany) at 40°C to eliminate the methanol. The extracts were then lyophilised and stored at -20°C until used. The yields were 12.34 g, 14.38 g, and 11.68 g, respectively, for the leaves (LE), stems (SE), and roots (RE). The powdered extracts were reconstituted with distilled water to the desired concentrations prior to use.

#### *Ocimum gratissimum*

The fresh leaves were harvested, processed and kept in the oven at 800 c for ten minutes to stop any enzyme activity and then at 600 c for 30 minutes. They were collected from the oven, air dried and ground into coarse power. 50g of the powdered leaves was stirred into 450 ml of boiling distilled water. Boiling was allowed to continue for five minutes, the mixture was then kept aside for thirty minutes to allow it to infuse. It was then filtered using a filter paper. The filtrate was concentrated to 200ml (1ml of the extract being equivalent to 0.25g of the starting material). The extract was kept in a refrigerator until it was time to use. Administration of extract Administration of the aqueous extract was done orally by means of calibrated syringe with attached rubber cannula. The animals received their doses daily for four weeks.

### 2.4. Insulin Treatment

Methods: Thirty male Wistar rats were randomly assigned into six groups (Group 1-non-diabetic control,

Group 2-streptozotocin-induced diabetic rats, Group 3-diabetic+ *O. gratissimum* extract, Group 4-diabetic+ *C. Citrasus*, Group 5-diabetic+ *O. gratissimum* and *C. Citrasus*. Group 6 given high-dose insulin [5-7U per day]. Throughout the four-week treatment, the body weight, non-fasting blood glucose concentration were monitored.

### 2.5. Diabetes Induction and Procedures

Diabetes was induced by a single intraperitoneal by injecting streptozotocin 40-60 mg/kg dissolved in a citrate-saline solution, pH 4.5, (Sigma, St. Louis, MO, USA) dissolved in sterile 0.9% saline. Rats were made to fast prior to the administration. After 12 h, a 10% glucose solution was offered to the animals to prevent hypoglycemia. After 72 h, blood samples were collected from the tail vein of the animals for evaluation of plasma glucose levels by the glucose-oxidase enzymatic method using Accu-Chek Advantage (Boehringer, Germany). Animals presenting glucose levels above 200 mg/ dL were included in the diabetic group. The animals presenting reversion of the signs of diabetes, i.e., those presenting glucose levels below 200 mg/dL, were excluded from this study. The examinations were repeated every 7 days to confirm maintenance of the glucose levels.

On the 28th day of post-treatment, the animals were fasted overnight, anesthetized with chloroform and sacrificed by humane decapitation. The blood was collected in sample tubes and serum collected and stored in deep-freezer prior to analysis. Meanwhile, fasting blood glucose was monitored weekly.

### 2.6. Assay of serum electrolytes

The concentrations of Na<sup>+</sup> and K<sup>+</sup> in the serum were determined by the flame photometry method Mac Donald, Serum chloride and calcium ion concentrations were determined using the method described by Schales and Schales, while bicarbonate ion concentration was estimated by a modified direct titration method as described by Sigaard-Anderson.

### 2.6.1. Determination of Serum Electrolytes (Sodium (Na<sup>+</sup>), Potassium (K<sup>+</sup>), Calcium (Ca<sup>++</sup>), Chloride (Cl<sup>-</sup>) & Creatinine in Rat Serum

The method as described in the manual for the Beckman Coulter Synchron® Clinical Systems and UniCel® Dx C 600, 800 (2004) systems. 40 µl of the sample was mixed in the ratio 1: 33 with the buffered solution. When the sample / buffer mixture made contact with the electrode, electrolytes ions in the sample underwent an ion exchange process with the corresponding ion in the hydrated portion of the electrode. Changes occur in the electrode potential as the ion exchange progresses, which are referenced to the reference electrode automatically by the system. The referenced potential follows the Nernst equation and is used to calculate the electrolyte ion concentration of the sample as follows:  $E = \text{Constant} + (\text{Slope}) (\log [\text{Ion}^+])$ .

### 2.7. Assay for Lipid Profile Estimation

**Sample Collection:** After 28 days of feeding with the modified diet, the animals were anesthetized using chloroform anesthesia. Blood sample was then collected by cardiac puncture for lipid profile analysis. A 5 ml syringe attached to 21 G needle was used to collect blood samples. The samples were collected into plain capped bottles and EDTA - treated bottles, for serum and whole blood samples respectively. The samples were immediately used for the analysis of lipid profile.

#### 2.7.1. Serum Lipid Profile Estimation

##### Estimation of Total Cholesterol (TC)

Serum total cholesterol (TC) was estimated using the enzymatic colorimetric test kit method of Siedel *et al.*, (1985). Cholesterol esterase catalyses the hydrolysis of cholesterol esters into free cholesterol and fatty acid. Cholesterol oxidase then catalyses the oxidation of the free cholesterol to cholestene-3-one and hydrogen peroxide. Phenol and 4-amino-antipyrine then combines with the hydrogen peroxide in the presence of peroxidase to produce a red coloured quinonemine which is read colorimetrically at 540nm. The total cholesterol concentration is directly proportional to the intensity of the colour obtained.

#### 2.7.2. Estimation of Serum Triacylglycerol (TG)

The triglyceride concentration in the samples was determined by method of Negele *et al.*, (1985). TGs are enzymatically hydrolyzed to glycerol and fatty acid by a lipoprotein lipase. Glycerol kinase then phosphorylates the glycerol produced to yield glycerol 3-phosphate, which is then oxidized to dihydroxyacetone phosphate and hydrogen peroxide by glycerol phosphate oxidase. The chromogen comprising of *n*-ethyl-n-sulphohydroxypropyl-*n*-foludine is then oxidized. A purple coloured quinoneimine dye formed as a result of these reactions was read colorimetrically at 540nm.

#### 2.7.3. Estimation of HDL-cholesterol (HDL-C)

HDL-cholesterol estimation was done according to the method of Siedel *et al.*, (1985) for total -cholesterol estimation previously described.

#### 2.7.4. Estimation of VLDL-cholesterol Concentration (VLDL-C)

The VLDL-C concentration was obtained by dividing the serum TG concentration by 5. This factor of 5 is based on the fact that in fasting subjects with triglyceride concentration of 400 mg/dl, the VLDL to total plasma triglyceride ratio is fixed at 1:5.  $\text{VLDL-C (mg/dl)} = \text{Triglyceride (TG)} / 5$ .

#### 2.7.5. Estimation of LDL-Cholesterol Concentration (LDL-C)

By the Friedewald's (1972) relationship, LDL-cholesterol is derived from the difference between the serum TC and sum of HDL-cholesterol and VLDL-cholesterol.  $\text{LDL-C} = \text{TC} - (\text{HDL-C} + \text{VLDL-C})$ .

### 2.8. Statistical Analysis

Significant differences between means of experiments were determined by least significant difference. SPSS 14.0 statistical tool was used to analyze the data obtained. Results were considered statistically significant at  $p < 0.05$  with Duncan's multiple range test.

### 3. RESULTS AND DISCUSSION

#### 3.1. Presentation of results in tables and charts

**Table 3.1. Daily Glucose Measurement in the test and control groups during the four-week study.**

s/n	groups	Treatment	Extract type		After 48 Hours	Week 1			Week 2			Week 3			Week 4		
Experimental Design				Baseline FBG (mmol/L)	Induced (mmol/L)	Treatment phase											
						Day 1	Day 3	Day 5	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5	Day 1	Day 3	Day 5
1	Negative control	Distilled water		5.8	5.7	5.6	5.7	5.6	5.6	5.7	5.6	5.6	5.6	5.5	5.6	5.6	5.7
2	Group 2	diabetic + 400mg/kg	O. gratissimum extract	5.3	15.1	14.5	12.2	11.6	10.2	10.0	8.4	7.7	7.2	6.7	5.6	5.2	5.2
3	Group 3	diabetic + 400mg/kg	C. citratum extract	5.4	15.2	14.5	14.3	13.8	12.1	10.2	10.0	9.6	8.1	8.0	7.2	6.5	5.8
4	Group 4	diabetic + 400mg/kg	O. gratissimum + C.citratum extract	5.8	16.2	16.2	14.8	12.6	12.1	11.6	10.3	9.6	8.2	7.7	5.7	4.7	4.5
5	Group 5	diabetic + 400mg/kg	Insulin	5.8	15.5	15.5	12.0	11.6	9.2	9.0	8.4	7.7	7.2	6.7	5.6	3.4	3.4

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.2. Assessment of Lipid Homeostasis in the test and control groups in the week 1 phase study.**

grouping	Treatment	Triglycerol (mg/dl ± sem)	Cholesterol (mg/dl ± sem)	High Density Lipoprotein (mg/dl ± sem)	Low density lipoprotein (mg/dl ± sem)
Negative control	(saline-treated)	120.05 ± 5.43	97.36 ± 2.24	85.24 ± 6.78	25.76 ± 3.46
Positive control	Diabetic (40mg/kg Streptozotocin)	190.28 ± 6.47*	148.13 ± 1.61*	34.33 ± 2.80	79.74 ± 1.96*
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	177.06 ± 5.91*	122.44 ± 2.99*	61.86 ± 2.25*	75.16 ± 2.80*
Diabetes + Extract 2	Cymbopogan. citratus (400mg/kg)	176.46 ± 11.09*	140.36 ± 6.01*	64.80 ± 0.90*	70.26 ± 6.01*
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	168.59 ± 5.79*	134.51 ± 3.61*	65.43 ± 1.69*	73.36 ± 2.06*
Diabetes + insulin	(5-7U/day)	158.89 ± 4.22*	137.25 ± 5.49*	64.38 ± 0.86*	77.08 ± 5.68*

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 4.3. Assessment of Lipid Homeostasis in the test and control groups in the week 2 phase study.**

grouping	Treatment	Triglycerol (mg/dl ± sem)	Cholesterol (mg/dl ± sem)	High Density Lipoprotein (mg/dl ± sem)	Low density lipoprotein (mg/dl ± sem)
Negative control	(saline-treated)	120.05 ± 5.43	97.36 ± 2.24	85.24 ± 6.78	25.76 ± 3.46
Positive control	Diabetic (100mg/kg Streptozotocin)	190.28 ± 6.47	148.13 ± 1.61	34.33 ± 2.80	79.74 ± 1.96
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	175.06 ± 4.41*	120.74 ± 3.69*	68.35 ± 3.24*	65.16 ± 2.80*
Diabetes + Extract 2	Cymbopogan .citratus (400mg/kg)	171.16 ± 6.09*	135.32 ± 6.51*	68.85 ± 3.14*	60.26 ± 6.01*
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	163.29 ± 3.19*	130.31 ± 4.41*	69.63 ± 1.59*	63.36 ± 2.06*
Diabetes + insulin	(5-7U/day)	158.89 ± 4.22*	131.21 ± 3.69*	68.24 ± 5.11*	67.08 ± 5.68*

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.4. Assessment of Lipid Homeostasis in the test and control groups in the week 3 phase study.**

grouping	Treatment	Triglycerol (mg/dl ± sem)	Cholesterol (mg/dl ± sem)	High Density Lipoprotein (mg/dl ± sem)	Low density lipoprotein (mg/dl ± sem)
Negative control	(saline-treated)	120.05 ± 5.43	97.36 ± 2.24	85.24 ± 6.78	25.76 ± 3.46
Positive control	Diabetic (100mg/kg Streptozotocin)	190.28 ± 6.47	148.13 ± 1.61	34.33 ± 2.80	79.74 ± 1.96
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	150.36 ± 3.21*	120.74 ± 5.12*	70.55 ± 6.22	45.06 ± 2.55
Diabetes + Extract 2	Cymbopogan .citratus (400mg/kg)	155.13 ± 4.63*	125.82 ± 4.51*	71.85 ± 3.14	40.46 ± 9.21
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	133.21 ± 3.31	120.31 ± 1.21*	79.63 ± 6.55	38.46 ± 2.56
Diabetes + insulin	(5-7U/day)	128.56 ± 4.22	101.21 ± 2.45	78.24 ± 7.06	30.68 ± 5.63

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.5. Assessment of Lipid Homeostasis in the test and control groups in the week 4 phase study.**

grouping	Treatment	Triglycerol (mg/dl ± sem)	Cholesterol (mg/dl ± sem)	High Density Lipoprotein (mg/dl ± sem)	Low density lipoprotein (mg/dl ± sem)
Negative control	(saline-treated)	120.05 ± 5.43	97.36 ± 2.24	85.24 ± 6.78	25.76 ± 3.46
Positive control	Diabetic (100mg/kg Streptozotocin)	190.28 ± 6.47	148.13 ± 1.61	34.33 ± 2.80	79.74 ± 1.96
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	130.46 ± 2.27*	100.74 ± 6.42	75.05 ± 7.02*	35.36 ± 2.55
Diabetes + Extract 2	Cymbopogan .citrus (400mg/kg)	135.53 ± 4.21*	105.72 ± 3.31	79.75 ± 3.77*	38.16 ± 8.31
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	123.03 ± 3.70	100.91 ± 1.43	81.43 ± 3.55	30.96 ± 2.66
Diabetes + insulin	(5-7U/day)	122.24 ± 4.44	100.21 ± 2.11	80.74 ± 5.06	28.78 ± 2.23

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.6a. Percentage Homeostatic re-alignment in Lipid Homeostasis in the test and control groups.**

grouping	Treatment	Triglycerol (mg/dl ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$	Cholesterol (mg/dl ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$
Negative control	(saline-treated)	120.05 ± 5.43	---	97.36 ± 2.24	---
Positive control	Diabetic (100mg/kg Streptozotocin)	190.28 ± 6.47	---	148.13 ± 1.61	---
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	130.46 ± 2.27*	-16.67	100.74 ± 6.42	-8.5
Diabetes + Extract 2	Cymbopogan. citratus (400mg/kg)	135.53 ± 4.21*	-25	105.72 ± 3.31	-19
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	123.03 ± 3.70	-5	100.91 ± 1.43	-8.5
Diabetes + insulin	(5-7U/day)	122.24 ± 4.44	-5	100.21 ± 2.11	-8.5

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.6b. Percentage Homeostatic re-alignment in Lipid Homeostasis in the test and control groups.**

grouping	Treatment	High Density Lipoprotein (mg/dl ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$	Low density lipoprotein (mg/dl ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$
Negative control	(saline-treated)	85.24 ± 6.78	---	25.76 ± 3.46	---
Positive control	Diabetic (100mg/kg Streptozotocin)	34.33 ± 2.80	---	79.74 ± 1.96	---
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	75.05 ± 7.02*	-24.3	35.36 ± 2.55	-20
Diabetes + Extract 2	Cymbopogan .citratus (400mg/kg)	79.75 ± 3.77*	-12.2	38.16 ± 8.31	-27
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	81.43 ± 3.55	-9.7	30.96 ± 2.66	-11
Diabetes + insulin	(5-7U/day)	80.74 ± 5.06	-9.7	28.78 ± 2.23	-6.7

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.7. Assessment of Electrolyte Homeostasis in the test and control groups in the week 1 phase study.**

grouping	Treatment	Na (mEq/L $\pm$ sem)	Cl (mEq/L $\pm$ sem)	K (mEq/L $\pm$ sem)
Negative control	(saline-treated)	142.42 $\pm$ 11.87	106.40 $\pm$ 6.03	105.77 $\pm$ 0.11
Positive control	Diabetic (100mg/kg Streptozotocin)	42.92 $\pm$ 8.67	56.48 $\pm$ 6.21	55.35 $\pm$ 5.13
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	89.65 $\pm$ 15.09*	99.44 $\pm$ 2.45*	68.07 $\pm$ 1.52*
Diabetes + Extract 2	Cymbopogon .citrus (400mg/kg)	104.74 $\pm$ 7.53*	94.02 $\pm$ 4.82*	66.37 $\pm$ 1.24
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citrus (400mg/kg each)	91.97 $\pm$ 15.73*	90.56 $\pm$ 6.34*	66.45 $\pm$ 3.71
Diabetes + insulin	(5-7U/day)	119.31 $\pm$ 5.02*	111.21 $\pm$ 12.12	65.67 $\pm$ 1.20***

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.8. Assessment of Electrolyte Homeostasis in the test and control groups in the week 2 phase study.**

grouping	Treatment	Na (mEq/L $\pm$ sem)	Cl (mEq/L $\pm$ sem)	K (mEq/L $\pm$ sem)
Negative control	(saline-treated)	142.42 $\pm$ 11.87	106.40 $\pm$ 6.03	105.77 $\pm$ 0.11
Positive control	Diabetic (100mg/kg Streptozotocin)	42.92 $\pm$ 8.67	56.48 $\pm$ 6.21	55.35 $\pm$ 5.13
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	90.55 $\pm$ 11.09*	100.04 $\pm$ 3.65	98.97 $\pm$ 8.52
Diabetes + Extract 2	Cymbopogon .citrus (400mg/kg)	115.44 $\pm$ 2.53*	102.52 $\pm$ 5.81	96.67 $\pm$ 8.24*
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citrus (400mg/kg each)	121.27 $\pm$ 9.43*	104.16 $\pm$ 4.34	86.05 $\pm$ 6.71*
Diabetes + insulin	(5-7U/day)	121.61 $\pm$ 4.42*	101.21 $\pm$ 7.16	95.66 $\pm$ 9.20*

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.9. Assessment of Electrolyte Homeostasis in the test and control groups in the week 3 phase study.**

grouping	Treatment	Na (mEq/L $\pm$ sem)	Cl (mEq/L $\pm$ sem)	K (mEq/L $\pm$ sem)
Negative control	(saline-treated)	142.42 $\pm$ 11.87	106.40 $\pm$ 6.03	105.77 $\pm$ 0.11
Positive control	Diabetic (100mg/kg Streptozotocin)	42.92 $\pm$ 8.67	56.48 $\pm$ 6.21	55.35 $\pm$ 5.13
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	92.85 $\pm$ 9.19*	100.24 $\pm$ 3.25	100.27 $\pm$ 8.52
Diabetes + Extract 2	Cymbopogon .citrus (400mg/kg)	120.42 $\pm$ 9.43*	105.42 $\pm$ 4.41	100.17 $\pm$ 0.24
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citrus (400mg/kg each)	124.77 $\pm$ 6.33*	105.16 $\pm$ 3.84	101.05 $\pm$ 6.91
Diabetes + insulin	(5-7U/day)	131.41 $\pm$ 6.42	105.81 $\pm$ 5.56	100.66 $\pm$ 7.70

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.10. Assessment of Electrolyte Homeostasis in the test and control groups in the week 4 phase study.**

grouping	Treatment	Na (mEq/L $\pm$ sem)	Cl (mEq/L $\pm$ sem)	K (mEq/L $\pm$ sem)
Negative control	(saline-treated)	142.42 $\pm$ 11.87	106.40 $\pm$ 6.03	105.77 $\pm$ 0.11
Positive control	Diabetic (100mg/kg Streptozotocin)	42.92 $\pm$ 8.67	56.48 $\pm$ 6.21	55.35 $\pm$ 5.13
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	102.75 $\pm$ 8.49*	102.28 $\pm$ 6.65	101.77 $\pm$ 9.22
Diabetes + Extract 2	Cymbopogon .citrus (400mg/kg)	130.72 $\pm$ 5.43*	105.92 $\pm$ 2.91	103.67 $\pm$ 7.28

<b>Diabetes + extracts 1 &amp; extract 2</b>	O. gratissimum + C. citratus (400mg/kg each)	134.97 ± 5.63	105.96 ± 8.54	102.85 ± 7.51
<b>Diabetes + insulin</b>	(5-7U/day)	141.31 ± 8.22	106.71 ± 8.16	104.46 ± 8.80

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.11. Percentage Homeostatic re-alignment in Electrolyte Homeostasis in the test and control groups.**

grouping	Treatment	Na (mEq/L ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$	K (mEq/L ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$	Cl (mEq/L ± sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$
<b>Negative control</b>	(saline-treated)	142.42 ± 11.87	---	105.77 ± 0.11	---	106.40 ± 6.03	---
<b>Positive control</b>	Diabetic (100mg/kg Streptozotocin)	42.92 ± 8.67	---	55.35 ± 5.13	---	56.48 ± 6.21	---
<b>Diabetes + Extract 1</b>	Ocimum gratissimum (400mg/kg)	102.75 ± 8.49*	-63.9	101.77 ± 9.22	-8.5	102.28 ± 6.65	-63.9
<b>Diabetes + Extract 2</b>	Cymbopogan. citratus (400mg/kg)	130.72 ± 5.43*	-18	103.67 ± 7.28	-4.3	105.92 ± 2.91	-18
<b>Diabetes + extracts 1 &amp; extract 2</b>	O. gratissimum + C. citratus (400mg/kg each)	134.97 ± 5.63	-18	102.85 ± 7.51	-6.4	105.96 ± 8.54	-18
<b>Diabetes + insulin</b>	(5-7U/day)	141.31 ± 8.22	-1.6	104.46 ± 8.80	-2.1	106.71 ± 8.16	-1.6

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.12. Assessment of Urea and Creatinine Homeostasis in the test and control groups in the week 1 phase study.**

grouping	Treatment	Urea ((mmol/L ± sem)	Creatinine (µmol/L ± sem)
<b>Negative control</b>	(saline-treated)	32.37 ± 3.26	62.69 ± 2.15
<b>Positive control</b>	Diabetic (100mg/kg Streptozotocin)	82.69 ± 2.15	169.27 ± 0.75
<b>Diabetes + Extract 1</b>	Ocimum gratissimum (400mg/kg)	79.98 ± 3.50*	169.50 ± 0.51*
<b>Diabetes + Extract 2</b>	Cymbopogan. citratus (400mg/kg)	78.41 ± 5.19*	168.13 ± 2.08*
<b>Diabetes + extracts 1 &amp; extract 2</b>	O. gratissimum + C. citratus (400mg/kg each)	70.43 ± 3.53*	164.76 ± 3.82*
<b>Diabetes + insulin</b>	(5-7U/day)	75.51 ± 3.74*	171.14 ± 1.49*

Values were presented as mean ± sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.13. Assessment of Urea and Creatinine Homeostasis in the test and control groups in the week 2 phase study.**

grouping	Treatment	Urea ((mmol/L ± sem)	Creatinine ((mmol/L ± sem)
<b>Negative control</b>	(saline-treated)	32.37 ± 3.26	62.69 ± 2.15
<b>Positive control</b>	Diabetic (100mg/kg Streptozotocin)	82.69 ± 2.15	169.27 ± 0.75
<b>Diabetes + Extract 1</b>	Ocimum gratissimum (400mg/kg)	59.56 ± 4.20*	109.10 ± 5.21*
<b>Diabetes + Extract 2</b>	Cymbopogan .citratus (400mg/kg)	58.61 ± 6.69*	108.63 ± 6.02*
<b>Diabetes + extracts 1 &amp; extract 2</b>	O. gratissimum + C. citratus (400mg/kg each)	50.13 ± 4.43*	104.09 ± 8.02*
<b>Diabetes + insulin</b>	(5-7U/day)	55.61 ± 7.04*	101.16 ± 5.09*

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.14. Assessment of Urea and Creatinine Homeostasis in the test and control groups in the week 3 phase study.**

grouping	Treatment	Urea ((mmol/L $\pm$ sem)	Creatinine ((mmol/L $\pm$ sem)
Negative control	(saline-treated)	32.37 $\pm$ 3.26	62.69 $\pm$ 2.15
Positive control	Diabetic (100mg/kg Streptozotocin)	82.69 $\pm$ 2.15	169.27 $\pm$ 0.75
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	49.08 $\pm$ 7.90	79.10 $\pm$ 5.21*
Diabetes + Extract 2	Cymbopogan. citratus (400mg/kg)	48.01 $\pm$ 3.79	78.23 $\pm$ 8.02*
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	40.93 $\pm$ 9.43	74.79 $\pm$ 6.02*
Diabetes + insulin	(5-7U/day)	45.51 $\pm$ 2.24	71.96 $\pm$ 0.09

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.15. Assessment of Urea and Creatinine Homeostasis in the test and control groups in the week 4 phase study.**

grouping	Treatment	Urea ((mmol/L $\pm$ sem)	Creatinine ((mmol/L $\pm$ sem)
Negative control	(saline-treated)	32.37 $\pm$ 3.26	62.69 $\pm$ 2.15
Positive control	Diabetic (100mg/kg Streptozotocin)	82.69 $\pm$ 2.15	169.27 $\pm$ 0.75
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	39.88 $\pm$ 8.92	69.50 $\pm$ 7.21
Diabetes + Extract 2	Cymbopogan .citratus (400mg/kg)	38.51 $\pm$ 8.72	67.83 $\pm$ 6.42
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	30.95 $\pm$ 8.13	64.69 $\pm$ 6.72
Diabetes + insulin	(5-7U/day)	35.91 $\pm$ 4.26	61.36 $\pm$ 4.69

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

**Table 3.16. Percentage Homeostatic re-alignment in Urea & Creatinine Homeostasis in the test and control groups.**

grouping	Treatment	Creatinine ((mmol/L $\pm$ sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$	Urea ((mmol/L $\pm$ sem)	% Homeostatic re-alignment $\frac{(V_a - V_{week\ 4})}{(V_b - V_{week\ 4})} \times 100$
Negative control	(saline-treated)	62.69 $\pm$ 2.15	---	32.37 $\pm$ 3.26	---
Positive control	Diabetic (100mg/kg Streptozotocin)	169.27 $\pm$ 0.75	---	82.69 $\pm$ 2.15	---
Diabetes + Extract 1	Ocimum gratissimum (400mg/kg)	69.50 $\pm$ 7.21	-7.1	39.88 $\pm$ 8.92	-18.6
Diabetes + Extract 2	Cymbopogan .citratus (400mg/kg)	67.83 $\pm$ 6.42	-4.9	38.51 $\pm$ 8.72	-16.3
Diabetes + extracts 1 & extract 2	O. gratissimum + C. citratus (400mg/kg each)	64.69 $\pm$ 6.72	-0.9	30.95 $\pm$ 8.13	-2.3
Diabetes + insulin	(5-7U/day)	61.36 $\pm$ 4.69	1.9	35.91 $\pm$ 4.26	-9.3

Values were presented as mean  $\pm$  sem. \* means values are statistically significant when compared to the negative control. N= 5.

### 3.2. Analysis of Results

#### Glucose Homeostasis

Table 4.1 presented the patterns of variations in glucose levels in the test and control groups before and after diabetes induction. Consequent upon treatments with the extracts of cymbopogon citratus and occimum gratissimum and insulin, It was demonstrated that occimum gratissimum significantly ( $p < 0.05$ ) reversed the diabetic glucose level of 15.2 mmol/L to 5.2 mmol/L at the end of four weeks, and cymbopogon citratus, significantly ( $p < 0.05$ ) from 15.2mmol/L to 5.4 mmol/L, while the mixture of both equally significantly ( $p < 0.05$ ) down-regulated the level of glucose from 16.2 mmol/L to 4.5 mmol/L. The anti-lipidemic potentials of these extracts were profoundly demonstrated. Although, occimum gratissimum seemed to be more effective when compared to cymbopogon citratus at the same dose. The effect of the combined dose of the extracts was aptly comparable to the standard drug insulin within the period of study.

#### Lipid Homeostasis

##### Triglycerides Homeostasis

The effect of different doses of cymbopogon citratus and occimum gratissimum on the rat triglycerides is demonstrated in Table 2. Mean level of triglycerides in the positive control group was  $190.28 \pm 6.47$  mg dL<sup>-1</sup>, which decreased significantly with the administration of different doses of cymbopogon citratus and occimum gratissimum (approximately 50%,  $p < 0.05$ ). The concentrations of triglycerides in the three experimental groups varied between 168 and 177mg/dL (week 1) and 123-130mg/dL (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of triglycerides as early as week 2 of the study and sustained decrementally till the fourth week of study. occimum gratissimum reduced the triglycerides from 177mg/dL (week 1) to 130.46mg/dL (week 4) in a more effective manner compared to the activity of cymbopogon citratus (176-135mg/dL). These regulatory potency in the extracts compared well with the insulin group under the same study period.

##### Cholesterol Homeostasis

The activities of the extracts of cymbopogon citratus and occimum gratissimum on the rat Cholesterol is demonstrated in Table 2. Mean level of Cholesterol in the positive control group was  $148 \pm 6.47$  mg dL<sup>-1</sup>, which decreased significantly with the administration of different doses of cymbopogon citratus and occimum gratissimum (approximately 30%,  $p < 0.05$ ). The concentrations of Cholesterol in the three experimental groups varied between 122 and 140mg/dL (week 1) and 100-105mg/dL (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of Cholesterol as early as week 2 of the study and sustained decrementally till the fourth week of study. occimum gratissimum reduced the Cholesterol from

122mg/dL (week 1) to 100.46mg/dL (week 4) in a more effective manner compared to the activity of cymbopogon citratus (140-105mg/dL). These regulatory potency in the extracts compared well with the insulin group under the same study period.

##### High Density Lipoprotein (HDL) Homeostasis

Table 4.2 and Figure 4.3 showed the effect of different doses of cymbopogon citratus and occimum gratissimum on the rat HDL level. Mean level of HDL in the positive control group was  $34.33 \pm 6.47$  mg dL<sup>-1</sup>, which increased significantly with the administration of different doses of cymbopogon citratus and occimum gratissimum (approximately 10%,  $p < 0.05$ ). The concentrations of HDL in the three experimental groups varied between 62 and 64mg/dL (week 1) and 75-80mg/dL (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic increment in the level of HDL as early as from week 2 of the study and sustained incrementally till the fourth week of study. (Figure 4.3). occimum gratissimum increased the HDL level from 62mg/dL (week 1) to 75mg/dL (week 4) in a more effective manner compared to the activity of cymbopogon citratus (65-79mg/dL). These regulatory potency in the extracts compared well with the insulin group under the same study period.

##### Low Density Lipoprotein (LDL) Homeostasis

Table 4.2 and Figure 4.4 revealed that the reducing effects of different doses of cymbopogon citratus and occimum gratissimum on the rat LDL were significantly demonstrated as shown. Mean level of LDL in the positive control group was  $79 \pm 1.76$  mg dL<sup>-1</sup>, which decreased significantly with the administration of different doses of cymbopogon citratus and occimum gratissimum (approximately 45%,  $p < 0.05$ ). The concentrations of LDL in the three experimental groups varied between 70 and 79mg/dL (week 1) and 28-38mg/dL (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of LDL as early as week 2 of the study and sustained decrementally till the fourth week of study. (Figure 4.4). occimum gratissimum reduced the LDL from 75mg/dL (week 1) to 35mg/dL (week 4) in a more effective manner compared to the activity of cymbopogon citratus (70-38mg/dL). These regulatory potency in the extracts compared well with the insulin group under the same study period.

##### Sodium ion Homeostasis

Table 4.3 and Figure 4.5 revealed that the boosting effects of different doses of cymbopogon citratus and occimum gratissimum on the rat Sodium ion were significantly demonstrated as shown. Mean level of Sodium ion in the positive control group was  $79 \pm 1.76$  mEq/L, which increased significantly with the administration of different doses of cymbopogon citratus and occimum gratissimum (approximately 20%,

$p < 0.05$ ). The concentrations of Sodium ion in the three experimental groups varied between 89 and 119 mEq/L (week 1) and 102-141 mEq/L (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic increase in the level of Sodium ion as early as week 2 of the study and sustained decrementally till the fourth week of study. (Figure 4.5). *occimum gratissimum* increased the Sodium ion from 89mg/dL (week 1) to 130 mEq/L (week 4) in a more effective manner compared to the activity of *cymbopogon citratus* 104-130 mEq/L). These regulatory potency in the extracts compared well with the insulin group under the same study period.

#### Chloride ion Homeostasis

Table 4.3 and Figure 4.5 showed that the boosting effects of different doses of *cymbopogon citratus* and *occimum gratissimum* on the rat Chloride ion were significantly demonstrated as shown. Mean level of Chloride ion in the positive control group was  $56 \pm 6.21$  mEq/L, which increased significantly with the administration of different doses of *cymbopogon citratus* and *occimum gratissimum* (approximately 50%,  $p < 0.05$ ). The concentrations of Chloride ion in the three experimental groups varied between 90 and 111 mEq/L (week 1) and 102-106 mEq/L (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of Chloride ion as early as week 2 of the study and sustained decrementally till the fourth week of study. *occimum gratissimum* reduced the Chloride ion from 99 mEq/L (week 1) to 105 mEq/L (week 4) in a more effective manner compared to the activity of *cymbopogon citratus* 94-105 mEq/L). These regulatory potency in the extracts compared well with the insulin group under the same study period.

#### Potassium ion Homeostasis

Table 4.6 and Figure 4.5 revealed that the boosting effects of different doses of *cymbopogon citratus* and *occimum gratissimum* on the rat Potassium ion level were significantly demonstrated as shown. Mean level of Potassium ion in the positive control group was  $55 \pm 5.13$  mEq/L, which increased significantly with the administration of different doses of *cymbopogon citratus* and *occimum gratissimum* (approximately 40%,  $p < 0.05$ ). The concentrations of Potassium ion in the three experimental groups varied between 65 and 68 mEq/L (week 1) and 102-104 mEq/L (week 4) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic increment in the level of Potassium ion as early as week 2 of the study and sustained incrementally till the fourth week of study. *occimum gratissimum* increased the Potassium ion from 75mg/dL (week 1) to 35 mEq/L (week 4) in a more effective manner compared to the activity of *cymbopogon citratus* 68-102 mEq/L). These regulatory potency in the extracts compared well with the insulin group under the same study period.

#### Urea Homeostasis

The activities of the extracts of *cymbopogon citratus* and *occimum gratissimum* on the rat Urea level was demonstrated in Table 4.10. Mean level of Urea in the positive control group was  $82 \pm 2.15$  mmol/L, which decreased significantly with the administration of different doses of *cymbopogon citratus* and *occimum gratissimum* (approximately 50%,  $p < 0.05$ ). The concentrations of Urea in the three experimental groups varied between 70 and 79 mmol/L (week 1) (Table 4.10) and 30-39 mmol/L (week 4) (Table 4.13) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of Urea as early as week 2 of the study and sustained decrementally till the fourth week of study. (Figure 4.10). *occimum gratissimum* reduced the Urea level from 79 mmol/L (week 1) to 39.46 mmol/L (week 4) in a more effective manner compared to the activity of *cymbopogon citratus* (78-38 mmol/L). These regulatory potency in the extracts compared well with the insulin group under the same study period.

#### Creatinine Homeostasis

The activities of the extracts of *cymbopogon citratus* and *occimum gratissimum* on the rat Creatinine level was demonstrated in Table 4.10. Mean level of Creatinine in the positive control group was  $169 \pm 0.75$  mmol/L, which decreased significantly with the administration of different doses of *cymbopogon citratus* and *occimum gratissimum* (approximately 75%,  $p < 0.05$ ). The concentrations of Creatinine in the three experimental groups varied between 164 and 171 mmol/L (week 1) (Table 4.10) and 61-69 mmol/L (week 4) (Table 4.13) which was statistically insignificant. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of Creatinine as early as week 2 of the study and sustained decrementally till the fourth week of study. (Figure 4.10). *occimum gratissimum* reduced the Creatinine level from 169 mmol/L (week 1) to 69 mmol/L (week 4) in a more effective manner compared to the activity of *cymbopogon citratus* (164-64 mmol/L). These regulatory potency in the extracts compared well with the insulin group under the same study period.

### 3.3 Discussion of Findings

The present investigation demonstrated that the selected plants individually and in combinations (*cymbopogon citratus* and *occimum gratissimum*) used in this study were effective in lowering cholesterol, Triglyceride and low density lipoprotein levels, while increasing the level of high density lipoprotein in streptozotocin-induced diabetic rats. It was equally demonstrated that these plants were significantly potent at regulating electrolyte homeostasis and regularizing the appropriate distributions of urea and creatinine in wistar rats under study. Their direct interference in the amelioration of disrupted glucose level in the blood was observed to be prompt and significant at the end of the first week and continued exponentially until the fourth week.

Table 4.1 presented the patterns of variations in glucose levels in the test and control groups before and after diabetes induction. Consequent upon treatments with the extracts of *cymbopogon citratus* and *occimum gratissimum* and insulin, It was demonstrated that *occimum gratissimum* significantly ( $p < 0.05$ ) reversed the diabetic glucose level at the end of four weeks, and *cymbopogon citratus*, significantly ( $p < 0.05$ ). The anti-lipidemic potentials of these extracts were profoundly demonstrated. Although, *occimum gratissimum* seemed to be more effective when compared to *cymbopogon citratus* at the same dose. The effect of the combined dose of the extracts was aptly comparable to the standard drug insulin within the period of study.

Epidemiological studies have also shown that high HDL-cholesterol levels could potentially contribute to antiatherogenicity, inhibit LDL-oxidation and protect endothelial cells from the cytotoxic effects of oxidized LDL [Assmann *et al.*, 2003]. The present result of oral administration of *cymbopogon citratus* and *occimum gratissimum* leaf extract caused significant declines in the blood levels of triglycerides, cholesterol, LDL, and increase HDL.

However, the mechanism by which *cymbopogon citratus* and *occimum gratissimum*, exhibit hypolipidemic role is unknown. It is probably that these plants changed the rate of fatty acids oxidation in the liver and reduced the rate of triglycerides biosynthesis in rats. Administered doses of *cymbopogon citratus* and *occimum gratissimum* on the rat decreased significantly the levels of triglyceride, Cholesterol and Low density lipoprotein. The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of these lipids as early as week 2 of the study and sustained decrementally till the fourth week of study. Although, *occimum gratissimum* reduced their levels in a more effective manner compared to the activity of *cymbopogon citratus*. These regulatory potency in the extracts compared well with the insulin group under the same study period.

The study revealed that the boosting effects of different doses of *cymbopogon citratus* and *occimum gratissimum* on the level of electrolytes were significantly demonstrated as shown in the results. The mixture of the two extracts more potently demonstrated the synergistic increase in the level of ions as early as week 2 of the study and sustained decrementally till the fourth week of study.

Oral administration of aqueous extract of *cymbopogon citratus* and *occimum gratissimum* leave extracts at a daily dose of 400 mg/kg for one week began to show significant changes in serum potassium, chloride and sodium levels with control. However, there was significant increase ( $P < 0.05$ ) two weeks, and until the fourth week. Cellular stability was achieved and maintained which compared well with the insulin-treated

group, if not, it could lead to alteration of the osmotic pressure of body fluid. This is due to the fact that abnormal concentration of sodium and/or potassium in serum can affect the osmotic pressure of the body fluid which is related to blood pressure (Healy, 1995; Cheesbrough, 2002). The relationship between sodium and diabetes is based on the capacity of this mineral to "attract" water. When the serum sodium level increase, the body retains water, thereby decreasing the serum sodium concentration.

Patients with DM often also have diminished kidney capacity to excrete  $K^+$  into urine. The combination of  $K^+$  shift out of cell and diminished urine  $K^+$  excretion causes hyperkalemia [Uribarri *et al.*, 1990].

Sodium is the major positive ion in fluid outside of cells. It regulates the total amount of water in the body and the transmission of sodium into and out of individual cells also plays a role in critical body function [Ezekwesili *et al.*, 2008].

Serum  $Na^+$  levels were observed to decrease significantly following diabetic induction. Glucose excretion in urine by diabetics imposes an osmotic diuresis or dehydration. With the consequence of electrolyte lost with dehydration in hyperglycemia the elevated serum glucose concentration result in high serum osmolarity, thus creating an osmolar gradient between the plasma compartment and the extracellular fluid leading to a shift of water into the intravascular space, the net effect is a dilution of the serum  $Na^+$  concentration resulting in hyponatremia [Liamis *et al.*, 2014].

A clear elevation of urea and creatinine in the diabetes group provided evidence that the induction of diabetes induced kidney injury. Administration of *occimum gratissimum* at 400 mg/kg concurrently with *cymbopogon citratus* significantly inhibited the rise in kidney injury markers, i.e., urea and creatinine. Creatinine is produced from the metabolism of protein in muscles, with most creatinine being filtered out of the blood by the kidney and excreted in urine.

The activities of the extracts of *cymbopogon citratus* and *occimum gratissimum* on the rat Urea and Creatinine levels was demonstrated in the study and their levels decreased significantly with the administration of different doses of *cymbopogon citratus* and *occimum gratissimum* (approximately 50%,  $p < 0.05$ ). The mixture of the two extracts more potently demonstrated the synergistic reduction in the level of Urea as early as week 2 of the study and sustained decrementally till the fourth week of study.

The glomerular filtration rate (GFR) is a well-known tool to measure the excretory capacity of the kidney. In clinical practice, GFR is obtained from the creatinine clearance in urine samples collected over 24 hours

[Adelman et al, 1981]. In renal disease, serum urea accumulates and causes uraemia because the rate of serum urea production exceeds the rate of clearance [Adeneye et al, 2008; Mayne, 1994].

It is very well known that urea reabsorption occurs as a consequence of the reabsorption of water, in another word, urea reabsorption varies markedly with the rate of urine flow and depends to the volume of water that is not reabsorbed (Fronzoza et al., 2004). While, creatinine is an organic base formed during muscle protein metabolism as a degradation product of creatine phosphate (Mayes, 1988). Lick many other organic bases, creatinine is filtered at the glomerulus and eliminated from plasma by the kidney. It means that creatinine is filtered only but is not reabsorbed, therefore ginger might have little influence on its excretion, whereas urea is filtered and reabsorbed partly in the nephrons. In addition the relation of urea to the water reabsorption may cause extra cellular contraction, which consequently resulted higher concentration of substances such as creatinine in plasma.

#### 4. CONCLUSION

The leaves of *cymbopogon citratus* and *occimum gratissimum* have showed enormous promises in the amelioration of associated anomalies in various homeostatic mechanisms involving glucose, lipids, electrolytes and kidney handling of urea and creatinine. The use of combination of the extracts at equal dose showed a much improved cellular recovery and homeostatic stability and balance in the space of four weeks of treatment which is what made the investigation somewhat novel in concept. These observations could prove that there is some degree of hope in the use of herbal approach in the management of metabolic diseases such as diabetes as demonstrated in the present study.

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