EFFECTS OF BLACK SEED *(NIGELLA SATIVA)* AND UZIZA LEAF *(PIPER GUINEENSE)* ON ELECTROLYTES, UREA AND CREATININE OF WISTAR ALBINO RATS

ABSTRACT

Aim: For centuries, plant and plant products have played a pivotal role in medication. This study evaluated the effect of aqueous extract of black seed (*Nigella sativa*) and uziza leaf (*Piper guineense)* on electrolytes, urea and creatinine of Wistar rats.

Materials and method: Twenty-five Wistar rats were used for the study, the rats were arranged into five groups with five rats in each of the groups. The rats had access to their normal feed but sucrose and margarine were used to induce hyperglycemia and hyperlipidemia respectively on the rats with the exception of the rats in the positive control group. The rats in the negative control were induced using the sucrose and margarine but were not treated using the aqueous extracts. The rats in the uziza group were treated with 2ml of uziza aqueous leaf extract, while the rats in the black seed group were treated with 2ml of black seed aqueous extract. The rats in the black seed and uziza leaf group were treated with 2ml of the combined aqueous extract.

Results: The results showed that the extracts had a decreasing effect which was time dependent on the electrolytes. The highest decrease was obtained on the third week of feeding when compared to the control (p=0.05). The sodium levels (mmol/L) showed for the negative control (198.23 ± 1.96), positive control (108.15 ± 1.60), uziza leaf (98.28 ± 4.17), black seed (101.67 ± 4.24), black seed and uziza (90.83 ± 2.14). The decrease for potassium levels (mEq/L) showed for the negative control (0.90 ± 0.06), positive control (0.05 ± 0.10), uziza leaf (0.07 ± 0.18), black seed (0.06 ± 0.19), black seed and Uziza (0.05 ± 0.10). Furthermore, the extracts also had a reducing effect on urea and creatinine levels with the highest reduction obtained on the third week (p=0.05). The urea levels (mmol/L) showed for the negative control (26.84 ± 0.05), positive control (15.15 ± 1.20), uziza leaf (12.83 ± 0.98), black seed (12.16 ± 2.01), black seed and uziza (11.48 ± 1.78). The extracts also decreased creatinine levels (mmol/L) with the negative control (284.58 ± 0.33), positive control (182.73 ± 3.67), uziza leaf (194.16 ± 18.30), black seed (167.34 ± 14.66), black seed and uziza (174.46 ± 10.66).

Conclusion: The extracts significantly decreased the elevated electrolytes levels and therefore uziza leaf and black seed can be used to restore kidney function.

Keywords: Creatinine, Electrolytes, *Nigella sativa, Piper guineense*, Potassium, Sodium, Urea,

1. INTRODUCTION

Naturally existing plants have been found to contain varieties of chemical substances which are of paramount importance to the medical world [1]. The use of natural products with therapeutic properties is as ancient as human civilization and for a long time, mineral, plant, and animal products were the main sources of drugs for therapeutic purpose [2]. Plants have always been a major source of nutrition and health care for both humans and animals. In recent years, there has been a growing interest in alternative therapies and the therapeutic use of natural products, especially those derived from plants [3].

Nigella sativa is commonly known as Black cumin in traditional medicine. *Nigella sativa* is a spice plant that is widely used for prevention and treatment of many ailments in many countries worldwide. It has been shown that the biological activity of the black cumin is related to the composition of its essential oil, which contains 30 to 48% of thymoquinone, 7 to 15% P-cymene, 6 to 12% carvacrol, 2 to 7% 4-terpineol, 1 to 4% Tanethole and 1 to 8% Sesquiterpene [4, 5]. Pharmacologically, thymoquinone and its derivatives are the most important components of Uziza or black pepper (*Piper guineese*) is a flowering plant in the family Piperaceae. The fruit, known as a peppercorn when dried, is a small drupe, five millimeters in diameter, dark red when fully matured, containing a single seed. It is a native to India and long been considered the world's most important spice. It is cultivated for its fruit, which is usually dried and used as a spice and seasoning [1] and also as preservative [6]. It is one of the most common spice in the European cuisine and has been known and prized since antiquity for both its flavor and its medicine [7]. Black pepper has been used to flavor foods for over 3000 years. The same fruit is also used to produce white pepper and green pepper [8]. The plant has a fruit which contains angular black seeds, and the seeds are considered to be the most valuable part contributing beneficial health effects. *Nigella sativa* as a natural remedy has been documented to possess numerous therapeutic values, including diabetes, tumour, hypercholesterolemia, hypertension, inflammation, and gastrointestinal disorders [9, 10].

In recent years, there has been a growing interest and demand in using medicinal plants for treating and preventing various diseases including cardiovascular diseases. Traditional medicines of plants origin have received much attention due to several factors such as easy availability, affordable cost, safety, and efficacy as well as cultural acceptability. Uziza leaf (*Piper guineense)* is an African plant with its leaves having a peppery taste and green when fresh and darker green when dried. *Piper guineense* contains over 700 species all over the world. It is a local spice mainly used in Nigerian dishes and it known to provide nutritional, culinary, insecticidal and medicinal benefits. It contains proteins, carbohydrates, alkaloids, steroids, glycosides, saponins, flavonoids, tannins and phenolic compounds; also vitamins, minerals and fat. The pharmacological properties of *N. sativa* is attributed to several component including proteins, amino acids, carbohydrates, fibers, oils (combination of fatty acids, especially polyunsaturated fatty acids), volatile oil (frequently thymoquinone), mineral, alkaloids, flavonoids, saponins, and others [11, 12, 13].

Uziza leaves have a peppery taste, are pale greenish color when fresh and darker green when frozen or dried. The inflorescence is a pedicel flower spike between 3 and 6 cm long and the peduncle 5 mm long. Flowers are greenish yellow and arranged in a spiral along the spine [14]. The fruits of *P.guineense* occur in clusters, small, reddish or reddish brown when ripe and black when dry. The fruit is a drupe, oval, 5mm in diameter [15, 16, 17].

P.guineense have been characterized and their chemical composition determined. They are used as therapeutic agents in minor ailments [18]. Phytochemicals are not vitamins or minerals but are bioactive compound found in plant foods that work with nutrient and dietary fibers to protect against disease [19]. The presence of phytochemicals like alkaloids in both the leaves and seed extracts of *P.guineense* signified the possession of medicinal properties within the plant. The flavonoids possess antioxidant, anti-inflammatory, anti-tumor, anti-allergic and antiplatelet properties [20]. They are also found to have cholesterol lowering ability. Alkaloids which are natural products present in *P.guineense* are made up of heterocyclic nitrogen that has anti-malarial, antihypertensive, antiarrhythmic and anticancer properties. Alkaloids are being used as central nervous system stimulant, powerful pain relievers, topical anesthetic in ophthalmology among others [21]. Tannins are compounds with proline-rich proteins that help to inhibit the absorption of iron when present in the gastrointestinal lumen thus reducing the bioavailability of iron due to the presence of compounds that help in the treatment of diseases like enteritis, gastritis, and esophagitis. Plants that contain tannins as their primary component are astringent, thus very beneficial for the management of diarrhea, dysentery, inflammation of the mucous membrane [22]. Saponins have anti-carcinogenic properties and may also play an important role in antimalarial activity of plants. *P.guineense* also contains cardiac glycosides in a significant amount and cardiac glycosides are useful in the management of diseases associated with the heart. *P.guineense* also contains dillapiol, 5-8% of piperine, elemicine, 10% of myristicine and safrole and these chemicals exhibit bactericidal and antimicrobial effects on some micro-organisms [23]. *P. guineense* like other members of the piper family contains 5-8% of the chemical "piperine" which gives them their "heat". They also contain large amounts of beta-carophyllene which is being investigated as an anti-inflammatory agent [24].

The kidneys are two bean-shaped organs in the renal system. They help the body pass waste as urine. They also help filter blood before sending it back to the heart. The kidneys perform many crucial functions, including: maintaining overall fluid balance, regulating and filtering minerals from blood, filtering waste materials from food, medications, and toxic substances, creating hormones that help produce red blood cells, promote bone health, and regulate blood pressure.

Blood urea nitrogen (BUN) provides a rough measurement of the glomerular filtration rate, the rate at which blood is filtered in the kidneys. Urea is formed in the liver as an end product of protein metabolism and is carried to the kidneys for excretion. Nearly all kidney diseases cause inadequate excretion of urea, elevating BUN levels in the blood. (Other causes of high BUN levels include gastrointestinal bleeding and steroid treatment). It can be done to determine the amount of urea nitrogen in the blood [25].

Creatinine is a breakdown product of creatine, an important component of muscle. The production of creatinine depends on muscle mass, which varies very little. Creatinine is excreted exclusively by the kidneys, and its level in the blood is proportional to the glomerular filtration rate. The serum creatinine level (serum is the clear liquid that remains after whole blood has clotted) provides a more sensitive test of kidney function than BUN because kidney impairment is almost the only cause of elevated creatinine. It can also be measured with a urine test. Creatinine clearance rate determines how efficiently the kidneys are clearing creatinine from the blood and serves as an estimate of kidney function. For renal function test, urine and serum levels of creatinine are measured, as well as the volume of urine excreted over a 24-hour period. The creatinine clearance rate is then calculated and expressed as the volume of blood, in milliliters, that can be cleared of creatinine in 1 minute. A low creatinine clearance value indicates abnormal kidney function. It requires both a urine and blood sample [25].

Sodium is one of the body's electrolytes, which are minerals that the body needs in relatively large amounts. Electrolytes carry an electric charge when dissolved in body fluids such as blood. Most of the body's sodium is located in blood and in the fluid around cells. Sodium helps the body keep fluids in a normal balance (see About Body Water). Sodium plays a key role in normal nerve and muscle function. The body obtains sodium through food and drink and loses it primarily in sweat and urine. Healthy kidneys maintain a consistent level of sodium in the body by adjusting the amount excreted in the urine. When sodium consumption and loss are not in balance, the total amount of sodium in the body is affected. The concentration of sodium in the blood may be too low (hyponatremia) or too high (hypernatremia) [25]

Potassium is one of the body's electrolytes, which are minerals that carry an electric charge when dissolved in body fluids such as blood. Most of the body's potassium is located inside the cells. Potassium is necessary for the normal functioning of cells, nerves, and muscles. The body must maintain the potassium level in blood within a narrow range. A blood potassium level that is too high (hyperkalemia) or too low (hypokalemia) can have serious consequences, such as an abnormal heart rhythm or even stopping of the heart (cardiac arrest). The body can use the large reservoir of potassium stored within cells to help maintain a constant level of potassium in blood.

The body maintains the right level of potassium by matching the amount of potassium consumed with the amount lost. Potassium is consumed in food and drinks that contain electrolytes (including potassium) and lost primarily in urine. Some potassium is also lost through the digestive tract and in sweat. Healthy kidneys can adjust the excretion of potassium to match changes in consumption. Some drugs and certain conditions affect the movement of potassium into and out of cells, which greatly influences the potassium level in blood [25].

The main aim of this study is to determine the effect of black seed (*Nigella sativa*) and uziza leaf (*Piper guineense*) on kidney profile (urea and creatinine) and electrolyte (sodium and potassium) of sucrose induced hyperglycaemia and margarine induced hyperlipidemia on Wilstar albino rats.

2. MATERIALS AND METHODS

Reagent kits were bought from Randox Laboratories Ltd. Ardmore, Diamond Road, Crumlin, Co. Antrim, United Kingdom BT29 4QY.

2.1. Experimental Animal and Design

Twenty five Wistar rats were purchased from the Biochemistry animal house in Choba University of Port Harcourt. The mean weight was 150±10g. The experimental animals were grouped into 5 groups with 5 rats in each group and the method of feed was by gavaging. The animals were acclimatized for one week.

GROUP 1: this group served as the positive control. This group had access to normal feed (ad libitum). They were not induced with sucrose and margarine. Furthermore, they were not treated with Uziza leaf and black seed extracts.

GROUP 2: this group served as negative control, it had 5 rats fed with normal feed (ad libitum) and distilled water but was induced with sucrose and margarine without treatment with either black seed or uziza leaf extract.

GROUP 3: this group contained 5 rats fed with normal feed (ad libitum) and distilled water, was induced with sucrose and margarine but treated with aqueous extract of black seed.

GROUP 4: this group contained 5 rats fed with normal feed (ad libitum) and distilled water was induced with sucrose and margarine but treated with aqueous extract of uziza leaf.

GROUP 5: this group contained 5 rats fed with normal feed (ad libitum) and distilled water was induced with sucrose and margarine but treated with equal proportion of the uziza leaf and black seed aqueous extracts.

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2.2. Sample Preparation

The black seed (*Nigella sativa*) was bought from a local market in Kaduna State, Nigeria, while the uziza leaf (*Piper guineense*) was obtained from a compound in Choba, Obio-Akpor Local Government area, Rivers State, Nigeria. The plants were identified as *Nigella sativa* and *Piper guineense* by a staff of the Department of Plant Science and Biotechnology, Faculty of Sciences University of Port Harcourt

50g of each of the samples; Uziza leaf (*Piper guineense*) and black seed (*Nigella sativa*), was soaked in 500ml of distilled water. After the stock preparation using a syringe, 2ml of the aqueous extract solution was collected and administered to the animals once daily. Also the feed used was formulated thus;

Table 1: Feed formulation table

	COMPOSITION BY WEIGHT (g)	COMPOSITION IN PERCENTAGE (%)
Normal feed	500	50
Margarine	200	20
Sucrose	200	20
Vitamin	100	10

2.3. Blood Collection

The animals after inducement with sucrose and margarine for one month were treated and sacrificed on a weekly bases. A desiccator with chloroform soaked cotton wool was used to weaken each of the animal put inside after some minutes, when properly anaesthetized it was brought out of the desiccator and dissected, some of the blood was put into a heparin bottle, fluoride oxalate and ethylene diamine tetra acetic acid (EDTA) bottle according to the parameters in consideration, the organs were also taken and put in a sterile bottle and all taken to the laboratory for analysis.

2.4. Determination of blood urea

Urease-glutamate dehydrogenase -UV method according to Berthelot's method [26] was used to determine the level of Urea in the samples. Mindray test kits was used for the analysis.

Reaction Principle

Urea + $H_2O_2 \leftrightarrow 2NH_4^+ + CO_3^{2-}$

α-Oxoglutarate + NH_4^+ + NADH↔ L-Glutamate + NAD^+ + H_2O

Urea is hydrolyzed by urease, and one of the products, ammonia, oxidises NADH to NAD^+ catalysed by glutamate dehydrogenase (GLDH). The absorbance decrease is directly proportional to the concentration of urea.

Procedure

Two test tubes labeled T1 (reagent blank) and T2 (test sample) were set up. T1 contained 1000 µL of reagent (R1) and 10 µL of distilled water, while T2 contained 1000 µL of reagent (R1) and 10 µL of test sample. The contents of each tube were mixed and incubated at 37°C for 2 min. After incubating, 250 µL of the second reagent (R2) was added to both test tubes. The contents of each tube was incubated again for 30 seconds at 37°C, the absorbance was read after 2 minutes at a wavelength of 546 nm.

Calculation

$\Delta A = [\Delta A \text{ sample}] - [\Delta A \text{ blank}]$

Conc. of urea = [change in absorbance of sample] – [change in absorbance of blank].

The result is expressed in mmol/L.

2.5. Determination of blood creatinine

Modified Jaffé method according to Bartels and Bohmer [27] was used to determine the level of creatinine in the samples. Mindray test kits was used for the analysis.

Reaction Principle

Creatinine + Picric acid ↔ Creatinine-Picric acid complex

At an alkaline solution, creatinine combines with picric acid to form an orange-red colored complex. The absorbance increase is directly proportional to the concentration of creatinine.

Procedure

Two test tubes labeled T1 (reagent blank) and T2 (test sample) were set up. T1 contained 180 µL of reagent (R1) and 18 µL of distilled water, while T2 contained 180 µL of reagent (R1) and 18 µL of test sample. The contents of each tube were mixed thoroughly at 37°C for 1 min. After incubating, 180 µL of the second reagent (R 2) was added to both test tubes. The content of the tube was mixed thoroughly, incubated at 37°C for 30 seconds and the absorbance read at 492 nm wavelength 2 minutes later.

Calculation

$\Delta A = [\Delta A \text{ sample}] - [\Delta A \text{ blank}]$

Conc. of creatinine = [change in absorbance of sample] – [change in absorbance of blank].

The result is expressed in mmol/L.

2.6. Determination of blood sodium

Sodium levels were determined by colorimetric test. Magnesium-uranyl acetate method. The Principle of this method is that after the precipitation of sodium magnesium-uranyl acetate, in the supernatant form with uranyl ions in solution with thioglycolic acid a yellow-brown coloured complex is formed. The optical density difference between the reagent blank (without precipitation of sodium) and the result of the analysis is proportional to the sodium concentration [28]. Reagent A kit contained uranylacetate (19mM) and magnesium acetate (140mM) while reagent B kit contained ammonium thioglycolate (550mM), ammonia (550mM) and the standard aqeous solution of sodium equivalent150mmol. 2.00ml of reagent A was mixed with 0.02 ml of the sample. For the standard, 2.00 ml of reagent A and 0.02 ml of the standard were mixed. The mixtures were let to stand for 5 minutes, they were then shaken thoroughly for 30 seconds. The mixtures were allowed to stand for 30 minutes. They were centrifuged at 2,000rpm for 5 minutes. The supernatant was then separated. 0.05ml of the clear supernatant was mixed with 2.00ml of reagent B. For the blank, 0.05 ml of reagent A and 2.00 ml of reagent B were mixed, while the standard tube contained 0.05 ml of supernatant and 2.00ml of reagent B. The absorbance of the mixtures was read after 10 minutes at 405nm with spectronic – 20 spectrophotometer.

Calculations: $$\frac{\text{Blank O.D} - \text{Sample O.D}}{\text{Blank O.D} - \text{Standard O.D}} \times 150 = \text{mmol/L}$$

2.7. Determination of potassium

Potassium levels were determined by colorimetric endpoint method [29]. One millilitre of reagent was mixed with 0.1ml of sample except for the controls, which had no samples. The blank tube contained 1.0ml of reagent while the standard tube contained 1.0ml of reagent and 0.1ml of standard. The mixtures were incubated at 25^{o}C for 3mins. The absorbance was read against reagent blank at 500nm with Spectronic -20 spectrophotometer.

$$\text{Calculations: } \frac{\Delta A \text{ unknown}}{\Delta A \text{ standard}} \times C \text{ standard} = \text{potassium concentration mEq/L}$$

2.8. Statistical Analysis

Data analysis was performed using the Statistical package for the Social Sciences software (SPSS, version 11.0). Data is displayed in mean ± SD. The statistical method of one way analysis of variance (ANOVA) was used to compare the mean values obtained among different groups. Differences were considered significant whenever the p-value is $p=0.05$.

3. RESULTS

TABLE 2: WEIGHT OF THE RATS BEFORE AND AFTER ADMINISTRATION OF THE EXTRACTS

Groups	Weight before administration (g)	Weight after administration (g)	Body weight change (g)
Negative control	66.33±13.22	117.18±20.79	50.85
Positive control	129.92±2.02	141.62±5.39	11.70
Uziza leaf	121.25±2.00	112.33±2.79	8.92
Black seed	105.53±0.19	81.54±4.14	23.94
Black seed & Uziza leaf	100.92±3.09	87.77±8.19	13.15

Results are expressed as mean ± standard deviation

Table 3: Effect of first, second & third week oral administration of Uziza leaf and black seed on sodium levels (Na) of Wistar rat.

	(mmol/L)		
Treatment	Week 1	Week 2	Week 3
Negative control	194.43 ± 3.15 ^{a}	195.95 ± 2.76^{b}	198.23 ± 1.96 ^{c}
Positive control	108.20 ± 3.08	108.60 ± 0.97	108.15 ±1.60
Uziza leaf	131.49 ± 8.95 ^{a}	120.73 ± 6.65 ^{b}	98.28 ± 4.17 ^{c}
Black seed	130.28 ± 7.87 ^{a}	122.95 ± 5.75 ^{b}	101.67 ± 4.24 ^{c}
Uziza & black seed	118.64 ± 7.16^{a}	100.17 ± 1.08 ^{b}	90.83 ± 2.14^{c}

Results are means of three determinations ± standard deviation.

^{abc} Different letters in a given row denote significant difference, p=0.05.

Table 4: Effect of first, second & third week oral administration of Uziza leaf and black seed on potassium levels (K) of Wistar rat.

	(mEq/L)		
Treatment	Week 1	Week 2	Week 3
Negative control	0.07 ± 0.08 ^{a}	0.08 ± 0.06 ^{b}	0.09 ± 0.06 ^{c}
Positive control	0.49 ± 0.05	0.05 ± 0.05	0.05 ± 0.10
Uziza leaf	0.05 ± 0.47 ^{a}	0.06 ± 0.50 ^{b}	0.07 ± 0.18 ^{c}

Black seed	0.04 ± 0.33 [a]	0.05 ± 0.23 [b]	0.06 ± 0.19 [c]
Uziza & black seed	0.52 ± 0.18[a]	0.51 ± 0.21 [b]	0.05 ± 0.10 [c]

Results are means of three determinations ± standard deviation.

[abc] Different letters in a given row denote significant difference, p=0.05.

Table 5: Effect of first, second and third week oral administration of Uziza leaf and black seed on Urea concentration on Wistar rat.

UREA CONCENTRATION (mmol/L)			
Treatment	Week 1	Week 2	Week 3
Negative control	26.18 ± 0.21 [a]	26.80 ± 0.09[b]	26.84 ± 0.05 [c]
Positive control	15.22 ± 0.60	15.27 ± 0.20	15.15 ± 1.20
Uziza leaf	18.43 ± 1.83 [a]	16.24 ± 0.57 [b]	12.83 ± 0.98 [c]
Black seed	18.37 ± 3.16 [a]	16.18 ± 0.88 [b]	12.16 ± 2.01 [c]
Uziza & black seed	16.14 ± 2.44[a]	15.00 ±0.78 [b]	11.48 ± 1.78[c]

Results are means of three determinations ± standard deviation.

[abc] Different letters in a given row denote significant difference, p=0.05.

Table 6: Effect of first, second and third week oral administration of Uziza leaf and black seed on Creatinine concentration of Wistar rat.

	(mmol/L)		
Treatment	Week 1	Week 2	Week 3
Negative control	285.27 ± 0.45	285.39 ± 0.23	284.58 ± 0.33
Positive control	194.44 ± 4.22	198.57 ± 2.53	182.73 ± 3.67
Uziza leaf	235.36 ± 23.18[a]	196.16 ± 10.80[b]	194.16 ± 18.30[c]
Black seed	210.53 ± 22.24[a]	198.26 ±11.88[b]	167.34 ± 14.66[c]
Uziza & black seed	195.80 ±16.38[a]	163.76 ± 12.14[b]	174.46 ±10.66[c]

Results are means of three determinations ± standard deviation.

[abc] Different letters in a given row denote significant difference, p=0.05.

4. RESULTS AND DISCUSSION

Table 3 shows the result of the effect of aqueous extract of uziza leaf and black seed on sodium level of Wistar rat. After three weeks of inducing the negative control group with sucrose and margarine without treatment, the value of 198.23 ± 1.96 mmol/L when compared with the positive control which was not induced 108.15 ± 1.60 mmol/L was obtained. The results showed that there was a significant effect on the kidney that led to the increase in the concentration of the plasma sodium (P<0.05). This agrees with the research by Igile et al. [30] stating that electrolyte abnormalities are common in diabetic patients and may be associated with increased morbidity and mortality. The disturbances of electrolyte homeostasis are also frequently observed in community subjects. Community-acquired electrolyte disorders, even chronic and mild, are related to poor prognosis [31]. Electrolyte disorders are usually multifactorial in nature. Various pathophysiological factors, such as nutritional status, gastrointestinal absorption capacity, coexistent acid-base abnormalities, pharmacological agents, other comorbid diseases (mainly renal disease) or acute illnesses, alone or in combination, play a key role.

Uziza group with value of 98.28 ± 4.17 mmol/L showed that uziza significantly decreased the concentration of the plasma sodium when compared to the negative control group at (P<0.05). The traditional and scientific relevance of *P. guineense* are numerous. It is endowed with therapeutic phytochemicals and nutrients which confer therapeutic effects on it and nutritional relevance as well [32]. Research has shown that *P. guineense* contains aromatic substances, alkaloids, salt and substitutes, another earlier report has shown that the leaf of *P. guineense* is rich in flavonoids and phenolic compounds and this compounds has been reported as being beneficial to the kidney electrolytes [33].

Black seed group with value of 101.67 ± 4.24 mmol/L also decreased the sodium levels. *Nigella sativa* have been used for thousands of years as a spice and food preservative, as well as a protective and curative remedy for several disorders [34]. Black seed extract, seed oil and the isolated bioactive compound thymoquinone possess significant non-toxic phytochemicals beneficial to health [34]. According to the previous and recent scientific researches carried out in various parts of the world, black seed is found effective in providing healing for 129 types of human ailments including 16 different types of cancer, diabetes, asthma, cold, hypertension, Alzeimer's disease, Parkinson's syndrome safety [35,36]. The black seed and uziza group with the value of 90.83 ± 2.14 mmol/L showed that the extract significantly decreased the elevated serum sodium concentration ($P<0.05$).

The extracts significantly reduced serum potassium levels ($p<0.05$) with uziza leaf (0.07 ± 0.18 mEql/L), black seed (0.06 ± 0.19 mEql/L), black seed and Uziza leaf (0.05 ± 0.10 mEql/L) when compared to the negative control group.

The extracts also showed reduction in serum urea levels with uziza leaf (12.83 ± 0.98) mmol/L, black seed (12.16 ± 2.01) mmol/L and the combination of black seed and Uziza leaf (11.48 ± 1.78) mmol/L ($p<0.05$). Also the extracts reduced the serum creatinine levels ($p<0.05$) with uziza leaf (197.16 ± 18.30) mmol/L, black seed (167.34 ± 14.66) mmol/L, black seed and Uziza leaf (174.46 ± 10.66) mmol/L. In a previous study it was shown that oral administration of aqueous extract of *N. sativa* seeds showed no significant changes in kidney function [37]. Another study also failed to show any toxicity for *N. sativa* fixed oil in mice [12, 38]. This study showed that oral administration of *N. sativa* has no toxicity by the concentration doses used. These results is in agreement with previous data reporting that *N. sativa* has a wide margin of safety [35, 36]. It also suggests that there are no toxic effect on kidney function of *N. sativa* at different doses a short period.

5. CONCLUSION

In conclusion, the extracts significantly decreased the elevated urea, creatinine and electrolytes levels and therefore uziza leaf and black seed can be used to restore kidney function. The results of the present study showed the absence of toxic effect of black seed and uziza leaf on rat kidney. Black seed and Uziza leaf are safe and effective herb that can be used by almost anyone. In general, the aqueous extract is not associated with serious side effects. No irritations or side effects are caused when the right dose is correctly applied.

Competing Interests

Authors have declared that no competing interests exist.

6. ETHICAL APPROVAL:

This research work was carried out with the approval of the University of Port Harcourt research ethics committee.

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