



## 32 1. INTRODUCTION

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

40 *Nigella sativa* is commonly known as Black cumin in traditional medicine. *Nigella sativa* is a  
41 spice plant that is widely used for prevention and treatment of many ailments in many countries  
42 worldwide. It has been shown that the biological activity of the black cumin is related to the  
43 composition of its essential oil, which contains 30 to 48% of thymoquinone, 7 to 15% P-cymene,  
44 6 to 12% carvacrol, 2 to 7% 4-terpineol, 1 to 4% Tanethole and 1 to 8% Sesquiterpene [4, 5].  
45 Pharmacologically, thymoquinone and its derivatives are the most important components of  
46 Uziza or black pepper (*Piper guineese*) is a flowering plant in the family Piperaceae. The fruit,  
47 known as a peppercorn when dried, is a small drupe, five millimeters in diameter, dark red when  
48 fully matured, containing a single seed. It is a native to India and long been considered the  
49 world's most important spice. It is cultivated for its fruit, which is usually dried and used as a  
50 spice and seasoning [1] and also as preservative [6]. It is one of the most common spice in the  
51 European cuisine and has been known and prized since antiquity for both its flavor and its  
52 medicine [7]. Black pepper has been used to flavor foods for over 3000 years. The same fruit is  
53 also used to produce white pepper and green pepper [8]. The plant has a fruit which contains  
54 angular black seeds, and the seeds are considered to be the most valuable part contributing  
55 beneficial health effects. *Nigella sativa* as a natural remedy has been documented to possess  
56 numerous therapeutic values, including diabetes, tumour, hypercholesterolemia, hypertension,  
57 inflammation, and gastrointestinal disorders [9, 10].

58

59 In recent years, there has been a growing interest and demand in using medicinal plants for  
60 treating and preventing various diseases including cardiovascular diseases. Traditional medicines

61 of plants origin have received much attention due to several factors such as easy availability,  
62 affordable cost, safety, and efficacy as well as cultural acceptability. Uziza leaf (*Piper guineense*)  
63 is an African plant with its leaves having a peppery taste and green when fresh and darker green  
64 when dried. *Piper guineense* contains over 700 species all over the world. It is a local spice  
65 mainly used in Nigerian dishes and it known to provide nutritional, culinary, insecticidal and  
66 medicinal benefits. It contains proteins, carbohydrates, alkaloids, steroids, glycosides, saponins,  
67 flavonoids, tannins and phenolic compounds; also vitamins, minerals and fat. The  
68 pharmacological properties of *N. sativa* is attributed to several component including proteins,  
69 amino acids, carbohydrates, fibers, oils (combination of fatty acids, especially polyunsaturated  
70 fatty acids), volatile oil (frequently thymoquinone), mineral, alkaloids, flavonoids, saponins, and  
71 others [11, 12, 13].

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

77 *P. guineense* have been characterized and their chemical composition determined. They are used  
78 as therapeutic agents in minor ailments [18]. Phytochemicals are not vitamins or minerals but are  
79 bioactive compound found in plant foods that work with nutrient and dietary fibers to protect  
80 against disease [19]. The presence of phytochemicals like alkaloids in both the leaves and seed  
81 extracts of *P. guineense* signified the possession of medicinal properties within the plant. The  
82 flavonoids possess antioxidant, anti-inflammatory, anti-tumor, anti-allergic and antiplatelet  
83 properties [20]. They are also found to have cholesterol lowering ability. Alkaloids which are  
84 natural products present in *P. guineense* are made up of heterocyclic nitrogen that has anti-  
85 malarial, antihypertensive, antiarrhythmic and anticancer properties. Alkaloids are being used as  
86 central nervous system stimulant, powerful pain relievers, topical anesthetic in ophthalmology  
87 among others [21]. Tannins are compounds with proline-rich proteins that help to inhibit the  
88 absorption of iron when present in the gastrointestinal lumen thus reducing the bioavailability of  
89 iron due to the presence of compounds that help in the treatment of diseases like enteritis,  
90 gastritis, and esophagitis. Plants that contain tannins as their primary component are astringent,

91 thus very beneficial for the management of diarrhea, dysentery, inflammation of the mucous  
92 membrane [22]. Saponins have anti-carcinogenic properties and may also play an important role  
93 in antimalarial activity of plants. *P.guineense* also contains cardiac glycosides in a significant  
94 amount and cardiac glycosides are useful in the management of diseases associated with the  
95 heart. *P.guineense* also contains dillapiol, 5-8% of piperine, elemicine, 10% of myristicine and  
96 safrole and these chemicals exhibit bactericidal and antimicrobial effects on some micro-  
97 organisms [23]. *P. guineense* like other members of the piper family contains 5-8% of the  
98 chemical “piperine” which gives them their “heat”. They also contain large amounts of beta-  
99 carophyllene which is being investigated as an anti-inflammatory agent [24].

100

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

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

112 Creatinine is a breakdown product of creatine, an important component of muscle. The  
113 production of creatinine depends on muscle mass, which varies very little. Creatinine is excreted  
114 exclusively by the kidneys, and its level in the blood is proportional to the glomerular filtration  
115 rate. The serum creatinine level (serum is the clear liquid that remains after whole blood has  
116 clotted) provides a more sensitive test of kidney function than BUN because kidney impairment  
117 is almost the only cause of elevated creatinine. It can also be measured with a urine test.  
118 Creatinine clearance rate determines how efficiently the kidneys are clearing creatinine from the  
119 blood and serves as an estimate of kidney function. For renal function test, urine and serum

120 levels of creatinine are measured, as well as the volume of urine excreted over a 24-hour period.  
121 The creatinine clearance rate is then calculated and expressed as the volume of blood, in  
122 milliliters, that can be cleared of creatinine in 1 minute. A low creatinine clearance value  
123 indicates abnormal kidney function. It requires both a urine and blood sample [25].

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

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

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

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

149

## 150 2. MATERIALS AND METHODS

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

### 153 2.1. Experimental Animal and Design

154

155 Twenty five Wistar rats were purchased from the Biochemistry animal house in Choba  
156 University of Port Harcourt. The mean weight was  $150\pm 10$ g. The experimental animals were  
157 grouped into 5 groups with 5 rats in each group and the method of feed was by oral gavage.  
158 The animals were acclimatized for one week.

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

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

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

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

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

172 .

173        **2.2.        Sample Preparation**

174

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

180    50g of each of the samples; Uziza leaf (*Piper guineense*) and black seed (*N.sativa*), was soaked  
181    in 500ml of distilled water. After the stock preparation using a syringe, 2ml of the aqueous  
182    extract solution was collected and administered to the animals once daily. Also the feed used was  
183    formulated thus;

184

UNDER PEER REVIEW

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187 **Table 1: Feed formulation table**

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

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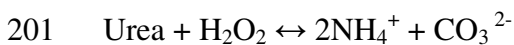
189 **2.3. Blood Collection**

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

197 **2.4. Determination of blood urea**

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

200 Reaction Principle





203 Urea is hydrolyzed by urease, and one of the products, ammonia, oxidises NADH to NAD<sup>+</sup>  
204 catalysed by glutamate dehydrogenase (GLDH). The absorbance decrease is directly  
205 proportional to the concentration of urea.

206 Procedure

207 Two test tubes labeled T1 (reagent blank) and T2 (test sample) were set up. T1 contained 1000  
208  $\mu\text{L}$  of reagent (R1) and 10  $\mu\text{L}$  of distilled water, while T2 contained 1000  $\mu\text{L}$  of reagent (R1) and  
209 10  $\mu\text{L}$  of test sample. The contents of each tube were mixed and incubated at 37°C for 2 min.  
210 After incubating, 250  $\mu\text{L}$  of the second reagent (R2) was added to both test tubes. The contents  
211 of each tube was incubated again for 30 seconds at 37°C, the absorbance was read after 2 minutes  
212 at a wavelength of 546 nm.

213 Calculation

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

215  $\text{Conc. of urea} = [\text{change in absorbance of sample}] - [\text{change in absorbance of blank}]$ .

216 The result is expressed in mmol/L.

## 217 2.5. Determination of **blood creatinine**

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

220 Reaction Principle

221  $\text{Creatinine} + \text{Picric acid} \leftrightarrow \text{Creatinine-Picric acid complex}$

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

224 Procedure

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

231 Calculation

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

233  $\text{Conc. of creatinine} = [\text{change in absorbance of sample}] - [\text{change in absorbance of blank}]$ .

234 The result is expressed in mmol/L.

235

236

## 237 **2.6. Determination of blood sodium**

238 Sodium levels were determined by colorimetric test. Magnesium-uranyl acetate method. The

239 Principle of this method is that after the precipitation of sodium magnesiumuranyl acetate, in

240 the supernatant form with uranyl ions in solution with thioglycolic acid a yellow-brown

241 coloured complex is formed. The optical density difference between the reagent blank

242 (without precipitation of sodium) and the result of the analysis is proportional to the sodium

243 concentration [28]. Reagent A kit contained uranylacetate (19mM) and magnesium acetate

244 (140mM) while reagent B kit contained ammonium thioglycolate (550mM), ammonia

245 (550mM) and the standard aqueous solution of sodium equivalent 150mmol. 2.00ml of reagent

246 A was mixed with 0.02 ml of the sample. For the standard, 2.00 ml of reagent A and 0.02 ml

247 of the standard were mixed. The mixtures were let to stand for 5 minutes, they were then

248 shaken thoroughly for 30 seconds. The mixtures were allowed to stand for 30 minutes. They

249 were centrifuged at 2,000rpm for 5 minutes. The supernatant was then separated. 0.05ml of

250 the clear supernatant was mixed with 2.00ml of reagent B. For the blank, 0.05 ml of reagent

251 A and 2.00 ml of reagent B were mixed, while the standard tube contained 0.05 ml of

252 supernatant and 2.00ml of reagent B. The absorbance of the mixtures was read after 10

253 minutes at 405nm with spectronic – 20 spectrophotometer.

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

255  $\text{Blank O.D} - \text{Standard O.D}$

256

257 **2.7. Determination of potassium**

258 Potassium levels were determined by colorimetric endpoint method [29]. One millilitre of  
259 reagent was mixed with 0.1ml of sample except for the controls, which had no samples. The  
260 blank tube contained 1.0ml of reagent while the standard tube contained 1.0ml of reagent and  
261 0.1ml of standard. The mixtures were incubated at 25°C for 3mins. The absorbance was read  
262 against reagent blank at 500nm with Spectronic -20 spectrophotometer.

263

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

265  $\Delta A \text{ standard}$

266

267

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269 **2.8. Statistical Analysis**

270 Data analysis was performed using the Statistical package for the Social Sciences software  
271 (SPSS, version 11.0). Data is displayed in mean  $\pm$  SD. The statistical method of one way analysis  
272 of variance (ANOVA) was used to compare the mean values obtained among different groups.  
273 Differences were considered significant whenever the p-value is **P=.05**.

274

275 **3. RESULTS**

276  
277 **TABLE 2: WEIGHT OF THE RATS BEFORE AND AFTER ADMINISTRATION OF**  
278 **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

279 Results are expressed as mean ± standard deviation

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**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 <sup>a</sup>	195.95 ± 2.76 <sup>b</sup>	198.23 ± 1.96 <sup>c</sup>
Positive control	108.20 ± 3.08	108.60 ± 0.97	108.15 ± 1.60
Uziza leaf	131.49 ± 8.95 <sup>a</sup>	120.73 ± 6.65 <sup>b</sup>	98.28 ± 4.17 <sup>c</sup>
Black seed	130.28 ± 7.87 <sup>a</sup>	122.95 ± 5.75 <sup>b</sup>	101.67 ± 4.24 <sup>c</sup>
Uziza & black seed	118.64 ± 7.16 <sup>a</sup>	100.17 ± 1.08 <sup>b</sup>	90.83 ± 2.14 <sup>c</sup>

285 **Results are means of three determinations** ± standard deviation.

286 <sup>abc</sup> Different letters in a given row denote significant difference, **p=0.05**.

287  
288

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

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

Black seed	0.04 ± 0.33 <sup>a</sup>	0.05 ± 0.23 <sup>b</sup>	0.06 ± 0.19 <sup>c</sup>
Uziza & black seed	0.52 ± 0.18 <sup>a</sup>	0.51 ± 0.21 <sup>b</sup>	0.05 ± 0.10 <sup>c</sup>

291 Results are means of three determinations ± standard deviation.

292 <sup>abc</sup> Different letters in a given row denote significant difference, P=0.05.

293

294

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

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

297 Results are means of three determinations ± standard deviation.

298 <sup>abc</sup> Different letters in a given row denote significant difference, p=0.05.

299

300

301 **Table 6: Effect of first, second & third week oral administration of Uziza leaf and black**  
 302 **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 <sup>a</sup>	196.16 ± 10.80 <sup>b</sup>	194.16 ± 18.30 <sup>c</sup>
Black seed	210.53 ± 22.24 <sup>a</sup>	198.26 ± 11.88 <sup>b</sup>	167.34 ± 14.66 <sup>c</sup>
Uziza & black seed	195.80 ± 16.38 <sup>a</sup>	163.76 ± 12.14 <sup>b</sup>	174.46 ± 10.66 <sup>c</sup>

303 Results are means of three determinations ± standard deviation.

304 <sup>abc</sup> Different letters in a given row denote significant difference, p=0.05.

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#### 308 4. DISCUSSION

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

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

330 Black seed group with value of  $101.67 \pm 4.24$  mmol/L also decreased the sodium levels. *Nigella*  
331 *sativa* have been used for thousands of years as a spice and food preservative, as well as a  
332 protective and curative remedy for several disorders [34]. Black seed extract, seed oil and the  
333 isolated bioactive compound thymoquinone possess significant non-toxic phytochemicals  
334 beneficial to health [34]. According to the previous and recent scientific researches carried out  
335 in various parts of the world, black seed is found effective in providing healing for 129 types of



336 human ailments including 16 different types of cancer, diabetes, asthma, cold, hypertension,  
337 Alzheimer's disease, Parkinson's syndrome safety [35,36]. The black seed and uziza group with  
338 the value of  $90.83 \pm 2.14$  mmol/L showed that the extract significantly decreased the elevated  
339 serum sodium concentration ( $P < 0.05$ ).

340 The extracts significantly reduced serum potassium levels ( $p < 0.05$ ) with uziza leaf ( $0.07 \pm 0.18$   
341 mEq/L), black seed ( $0.06 \pm 0.19$  mEq/L), black & Uziza ( $0.05 \pm 0.10$  mEq/L) when compared  
342 to the negative control group.

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

## 353 5. CONCLUSION

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

## 360 Competing Interests

361 Authors have declared that no competing interests exist.

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363

364 **6. ETHICAL APPROVAL:**

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

367

368

369 **REFERENCE**

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