



Contents lists available at ScienceDirect

Journal of Traditional and Complementary Medicine

journal homepage: <http://www.elsevier.com/locate/jtcm>

## Effects of ethanolic extracts of leaf, seed and fruit of *Datura metel* L. on kidney function of male albino rats

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### ARTICLE INFO

#### Article history:

Received 10 August 2016  
Received in revised form  
1 September 2017  
Accepted 2 September 2017  
Available online 28 September 2018

#### Keywords:

*Datura metel*  
Electrolytes  
Histology  
Inflammation  
Kidney

### ABSTRACT

Effects of ethanolic extracts of leaf, seed and fruit of *Datura metel* on kidney function of male albino rats was investigated in this study. The result showed a non-significant ( $p > 0.05$ ) increase of urea concentration in groups 2 and 3 administered low (300 mg/kg bw) and high (600 mg/kg bw) dose of leaf extract respectively and a non-significant ( $p > 0.05$ ) decrease in all groups administered the seed and fruit extracts compared with normal control (group 1). Creatinine increased significantly ( $p < 0.05$ ) in groups 4 and 7 administered low dose (300 mg/kg bw) of seed extract and high dose (600 mg/kg bw) of fruit extract respectively, but increased non-significantly in other groups (2, 3, 5 & 6) compared with normal control. Sodium, potassium and bicarbonate concentrations increased non-significantly ( $p > 0.05$ ) in all groups administered the various extracts, except in group 4 in which sodium reduced non-significantly ( $p > 0.05$ ) compared with normal control. Chloride increased significantly ( $p < 0.05$ ) in group 5 and non-significantly ( $p > 0.05$ ) in groups 3, 6 and 7, but reduced non-significantly ( $p > 0.05$ ) in group 4 compared with normal control. The administration of some of the extracts in comparison with the normal control in histology of the animals show glomerular extrusion and glomerular collapse with resultant increased urinary space, dilated tubules, vacuolations in some epithelial lining of most of the tubules in the medulla and inflammatory cellular infiltration at some peritubular regions. The results showed that some parts of *Datura metel* posed mild negative effects, while some parts could possess nephroprotective potential by regulating the kidney function of male albino rats.

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## 1. Introduction

Over the past decade, there has been a resurgence of interest in the investigation of natural materials as a source of potential drug substance.<sup>1,2</sup> Plants have great potential for the treatment and management of some diseases and have been used in many countries for the treatment of different diseased conditions. The medicinal value of plants lies in their bioactive phytochemical constituents that produce definite physiological actions in the human body<sup>3</sup> and other animals. The chemical constituents include flavonoids, alkaloids, essential oils, saponins, terpenoids, tannins,

phenolic compounds, etc. Many medicinal plants contain some chemical constituents that could cause harmful effects to humans if taken in large quantities. Alkaloids occurring in a large amount could make plants poisonous despite its medicinal effects. Most countries are now applying traditional medicinal systems that involve the use of herbal drugs and remedies. Many have incorporated plants as a source of medicinal agents into their primary modality of health care.<sup>1,2</sup>

*Datura metel* L. is a member of the plant family Solanaceae. Its common names are: Thorn apple, Devil's apple, Jimson weed and Angel's trumpet. Its indigenous names in Nigeria include: Igbo – Myaramuo; Hausa – Zakami; Yoruba – Apikan.<sup>4</sup> It is native to Asia and Africa, widely cultivated and naturalized in the tropics. *Datura metel* is a herbaceous, leafy plant and can grow up to 200 cm in height. The leaves are alternate and can be up to or more than 26 cm long and 21 cm wide. The fruit can contain up to 300 or more

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Peer review under responsibility of The Center for Food and Biomolecules, National Taiwan University.

seeds, splitting open when it is ripened to release the numerous seeds. In many parts of Nigeria, especially in the northern part, *Datura metel* is found growing as a weed in abandoned farmlands and/or dumpsites, but it is sometimes cultivated. Different parts (leaves and seeds) of the plant can be used for many purposes and in several ways mostly for its psychoactive activities.<sup>5</sup> This could make the different parts of *Datura metel* to be abused by some youths who are more users and are prone to dangers of smoking and drug abuse. The extract of *Datura*, however, is a potent poison and the indiscriminate use of the plant parts may lead to delirium and acute poisoning that may lead to death. The active constituents in *Datura metel* include scopolamine, atropine, hyoscyamine, withanolides (lactones) and other tropanes. Nuhu (2002)<sup>6</sup> reported that *D. metel* contains tropane alkaloids and are used as sedative, anti-spasmodic and mydriatic agents.

Atropine binds competitively to muscarinic receptors blocking parasympathetic cholinergic neurons. It acts on both peripheral and central muscarinic receptors. In lower doses, it affects cardiovascular system causing bradycardia. Atropine increases acetylcholine release and hence used as an antidote to treat organophosphate poisoning and to reduce the gastrointestinal activity.<sup>7</sup> Withanolide compounds have been reported to show significant antitumor, cytotoxic, anti-inflammatory, antibacterial, hepatoprotective, sedative, cytostatic and immunosuppressive activity.<sup>8</sup> Hyoscyamine and scopolamine act as anti-muscarinic compounds and act on both central nervous system (CNS) and peripheral nervous system. Scopolamine is used as CNS depressant in small doses and used to treat motion sickness. Apart from this, other therapeutic implications include antiemetic, antidysmenorrhea, and gastric antispasmodic. Hyoscyamine is used as an adjunct in Zollinger-Ellison syndrome.<sup>8</sup> Typical findings in *Datura* poisoning are dryness of the mouth, thirst, fever, amnesia, urinary retention, decreased salivation, papillary dilation, tachycardia, hallucinations, palpitation, ataxia, delirium leading to coma, cardiac and respiratory arrest and death.<sup>8</sup>

*Datura metel* is believed to be a medicinal plant widely used in phytomedicine to cure diseases such as asthma, cough, convulsion and insanity. Various parts of the plant (leaves, seeds, roots and fruits) are used for different purposes in herbal medicine. All parts of *Datura metel* (especially the leaves and seed) are believed to have anaesthetic, hallucinogenic, anti-asthmatic, anti-spasmodic, anti-tussive, narcotic, bronchodilator, hypnotic and mydriatic effects. The leaves are used as a local application for treating rheumatic swellings of the joints, lumbago, sciatica, neuralgia, painful tumors, scabies, eczema, allergy and glandular inflammations, such as mumps; used externally for earache and smoked to relieve spasmodic asthma. Seeds are used externally for piles.<sup>9</sup> The seeds, leaves and roots are reported to be used in insanity, fever with catarrh, diarrhoea, skin diseases and cerebral complications.<sup>10</sup>

The aim of the present study is to investigate the effects of ethanolic extracts of leaf, seed and fruit of *Datura metel* on kidney function of male Albino rats. The results obtained will help to reveal and establish the likely effects of these plant parts on kidney function of consumers or users of *Datura metel*.

## 2. Materials and methods

### 2.1. Plant materials

The leaves, seeds and fruits of *Datura metel* were harvested at the Wapan-Nghaku, Wukari, Taraba State, Nigeria. The plant materials (leaves, seeds and fruits) were rinsed and then sun-dried. The dried leaves, seeds and fruits were milled to powder. Known weights of the powders were extracted with 70% ethanol by cold maceration for 48 h and filtered. The filtrates were evaporated to dryness. The concentrations of the extracts were made in normal saline for the experiment.

### 2.2. Experimental animals

Thirty-five (35) healthy male albino rats, aged 8 weeks were used in this study. The animals were purchased from Vom, Plateau State and kept in the Animal House, Department of Biochemistry, Faculty of Pure and Applied Sciences, Federal University Wukari, Taraba State, Nigeria. They were allowed to acclimatize for 7 days under the Institutional standard laboratory conditions for experimental animal with free access to commercial rat feed and water.

### 2.3. Experimental design

The animals were randomly placed into seven (7) groups of five (5) rats in each group. Group 1 served as the normal control (it received a placebo of normal saline). Group 2 and 3 received 300 mg/kg b.w. and 600 mg/kg b.w. of leaf extract respectively. Group 4 and 5 received 300 mg/kg b.w. and 600 mg/kg b.w. of seed extract respectively, while group 6 and 7 received 300 mg/kg b.w. and 600 mg/kg b.w. of fruit extract respectively. The test animals (groups 2, 3, 4, 5, 6 and 7) received the extracts as stated above for seven consecutive days. The extracts were administered through oral route (using gavage intubation). All animals were allowed access to feed and water *ad libitum* throughout the study.

### 2.4. Blood collection

After 24 h of administration of the extracts of *Datura metel*, the animals were starved overnight, anaesthetized with chloroform and sacrificed. Blood was collected by cardiac puncture from each animal into clean sample bottle. The blood sample was allowed to stand for about 15 min to clot and further spun in a centrifuge at 4000 rpm for 10min. Serum was separated from the clot with Pasteur pipette into sterile sample tubes for the measurement of kidney function parameters.

### 2.5. Biochemical analysis

Serum creatinine and serum urea were determined using auto-analyser: Selectra ProM, while serum concentrations of sodium, potassium, chloride and bicarbonate were determined using an electrolyte auto-analyser: Landwind LW E60B.

**Table 1**  
Concentrations of urea and creatinine (mmol/L).

Parameters	Group 1 (Normal control)	Group 2 (leaf: 300 mg/kg bw)	Group 3 (leaf: 600 mg/kg bw)	Group 4 (seed: 300 mg/kg bw)	Group 5 (seed: 600 mg/kg bw)	Group 6 (fruit: 300 mg/kg bw)	Group 7 (fruit: 600 mg/kg bw)
Urea	6.33 ± 1.30	7.13 ± 1.53	6.35 ± 0.76	5.55 ± 0.55	5.60 ± 0.51	5.20 ± 0.50	5.75 ± 0.99
Creatinine	63.13 ± 3.50*	80.18 ± 17.71	69.65 ± 7.55	87.90 ± 8.55*	77.00 ± 15.74	74.65 ± 11.57	91.93 ± 6.34*

Results represent mean ± standard deviation of group results obtained (n = 5).

Mean in the same row, having \* are statistically significant (p < 0.05) compared with the normal control (group one).

**Table 2**  
Concentrations of serum electrolytes (mmol/L).

Parameters	Group 1 (Normal control)	Group 2 (leaf: 300 mg/kg bw)	Group 3 (leaf: 600 mg/kg bw)	Group 4 (seed: 300 mg/kg bw)	Group 5 (seed: 600 mg/kg bw)	Group 6 (fruit: 300 mg/kg bw)	Group 7 (fruit: 600 mg/kg bw)
Na <sup>+</sup>	137.75 ± 1.42	139.70 ± 2.06	138.70 ± 1.09	136.90 ± 0.66	138.35 ± 2.04	138.90 ± 0.62	138.25 ± 0.91
K <sup>+</sup>	4.43 ± 0.26	5.05 ± 0.39	5.45 ± 0.82	4.63 ± 0.29	4.68 ± 0.19	4.88 ± 0.30	4.45 ± 0.39
Cl <sup>-</sup>	104.75 ± 1.26*	104.75 ± 2.63	106.25 ± 2.21	104.25 ± 1.90	107.75 ± 1.71*	105.50 ± 2.38	106.75 ± 1.71
HCO <sub>3</sub> <sup>-</sup>	24.50 ± 1.29	27.00 ± 2.16	26.00 ± 1.83	24.51 ± 1.29	27.00 ± 2.16	25.50 ± 1.29	27.00 ± 1.83

Results represent mean ± standard deviation of group results obtained (n = 5).

Mean in the same row, having \* is statistically significant (p < 0.05) compared with the normal control (group one).

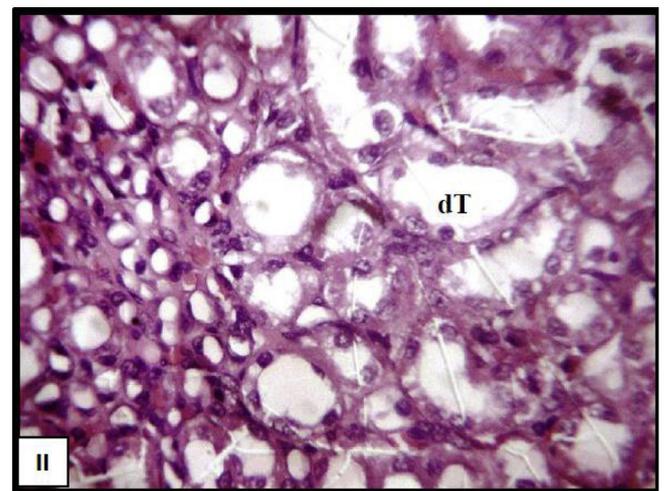
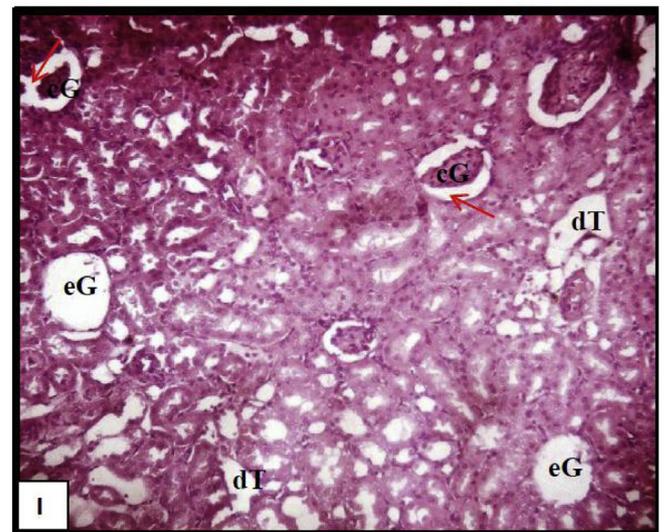
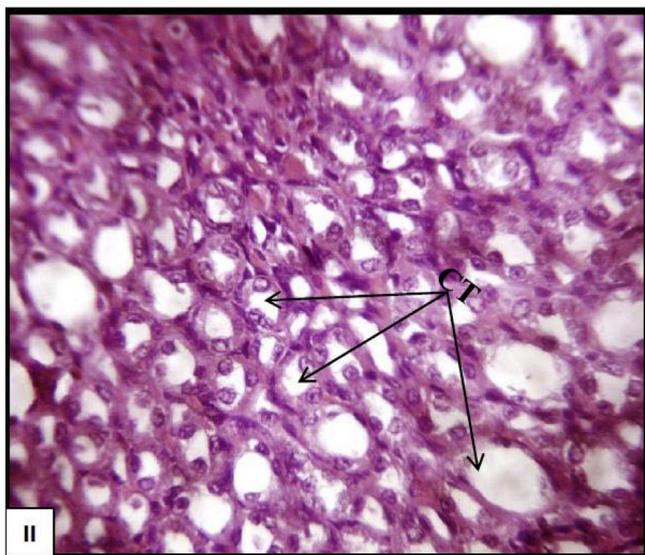
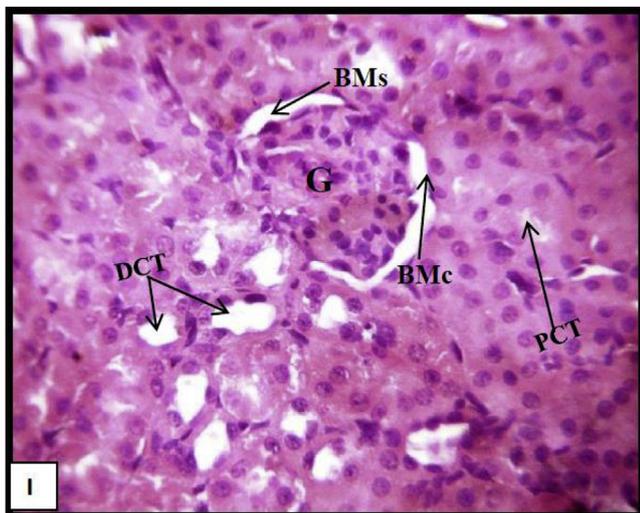
Legend: Na<sup>+</sup> = Sodium, K<sup>+</sup> = Potassium, Cl<sup>-</sup> = Chloride, HCO<sub>3</sub><sup>-</sup> = Bicarbonate.

## 2.6. Histological analysis

After animal sacrifice, the kidneys of each of the seven groups were taken and examined histologically.

## 2.7. Statistical analysis

Statistical analysis was carried out with the use of standard Student-T-distribution test: using Statistical Package for Social Sciences (SPSS) version 21 and group means were compared for significance at p ≤ 0.05. Data were presented as mean ± standard deviation (n = 5).



**Plate 1.** Photomicrographs of the cortex [I] and medulla [II] of Kidney section from normal control rat (group 1) showing normal histoarchitecture of the cortical (I) and medullary (II) portions of the renal tissue. The glomerulus (G), cortical and medullary tubules, Bowman's capsule (BMc) and space (BMs) appear normal. [PCT: Proximal Convoluted Tubule; DCT: Distal Convoluted Tubule; CT: Collecting tubules] (Stain: H&E; Mag: I&II-x400).

**Plate 2.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 300 mg/kg bodyweight of *Datura metel* leaf extract (group 2). In the cortex, glomerular extrusion (eG) and glomerular collapse (cG) with resultant increased urinary space (red arrows) are observed. The tubules however, appear dilated (dT). (Stain: H&E; Mag: I-x100; II-x400).

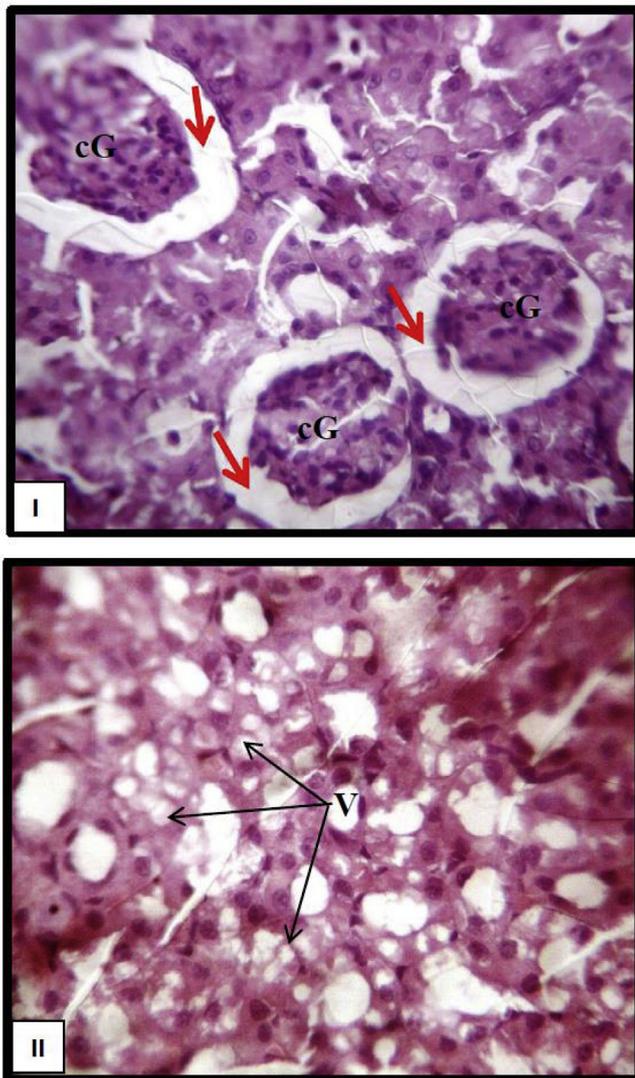
### 3. Results and discussion

The kidneys perform lots of functions in animals such as homeostasis and acid-base balance, regulation of the balance of electrolytes in the blood, removal of waste products of metabolism, secretion of some enzymes and hormones, metabolism and osmoregulation. Any alteration or abnormality associated with the kidneys could lead to non-performance or inefficiency in carrying-out these functions by the kidney. The abnormalities associated with kidney function could be ascertained by evaluating the levels of some kidney function parameters such as blood urea, creatinine, serum electrolytes and also histological examination of the organ, among others.

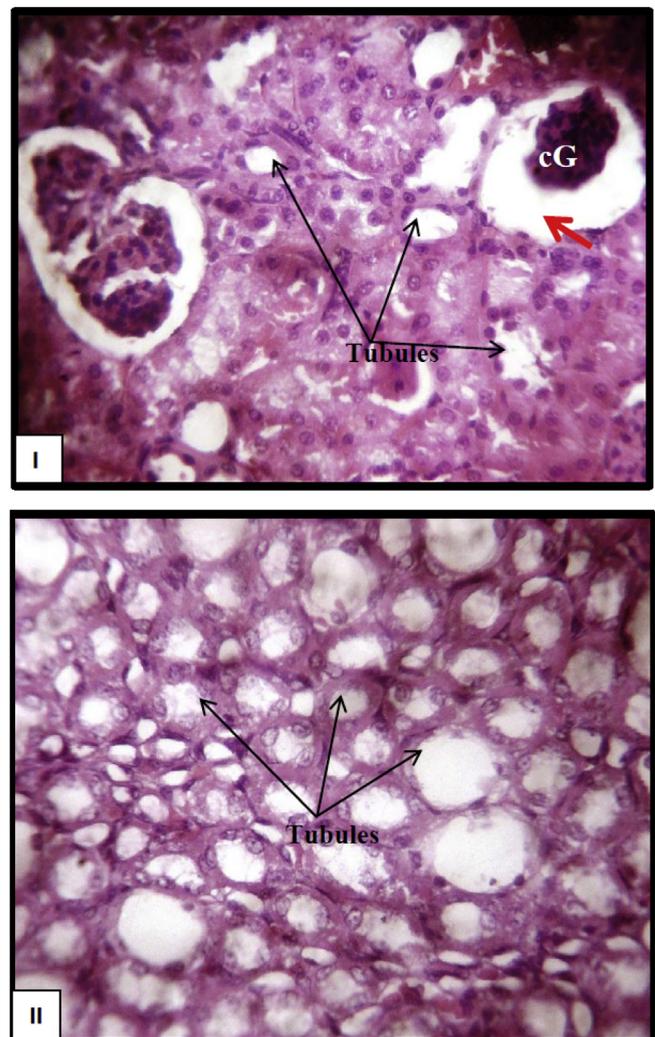
The results of this study show that serum urea level increased non-significantly in the group of animals administered the leaf extracts, while it decreased non-significantly in the groups administered the seed extract and the fruit extract when compared with the normal control (Table 1). This increase and decrease is a sign of alteration and could possibly result from the effects of the

extracts administered, thereby altering the rate at which the kidney excretes urea. Urea is the final degradation product of protein and amino acid metabolism. It is synthesized in the liver from ammonia produced as a result of deamination of proteins. Filtration of urea from the blood into the urine by the renal glomeruli is the major means by which excess nitrogen is eliminated from the body. Among the renal causes of increased urea levels are acute glomerulonephritis, chronic nephritis, polycystic kidney, nephrosclerosis, and tubular necrosis. Any type of obstruction of the urinary tract is a post-renal cause for elevated BUN levels.<sup>11</sup> Other causes of increased level of urea is cardiac decompensation, water depletion due to decreased intake and excessive loss, increased protein catabolism and high protein diet. Elevation of urea level was mostly recorded in group two animals administered low concentration of the leaf extract, while reduction in urea level was recorded in the groups administered the seed extract and fruit extract (Table 1). Both urea and creatinine are cleared by the renal glomeruli, however, urea is subsequently partially reabsorbed by the renal tubules, while creatinine is not.

Creatinine level in all groups administered the different extracts obviously increased when compared with the normal control.



**Plate 3.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 600 mg/kg bodyweight of *Datura metel* leaf extract (group 3). The glomeruli in the cortical region appear collapsed with evidence of increased urinary space (red arrows). Vacuolations (V) in the epithelial lining of most of the tubules in the medulla (II) are shown. (Stain: H&E; Mag: I&II-x400).

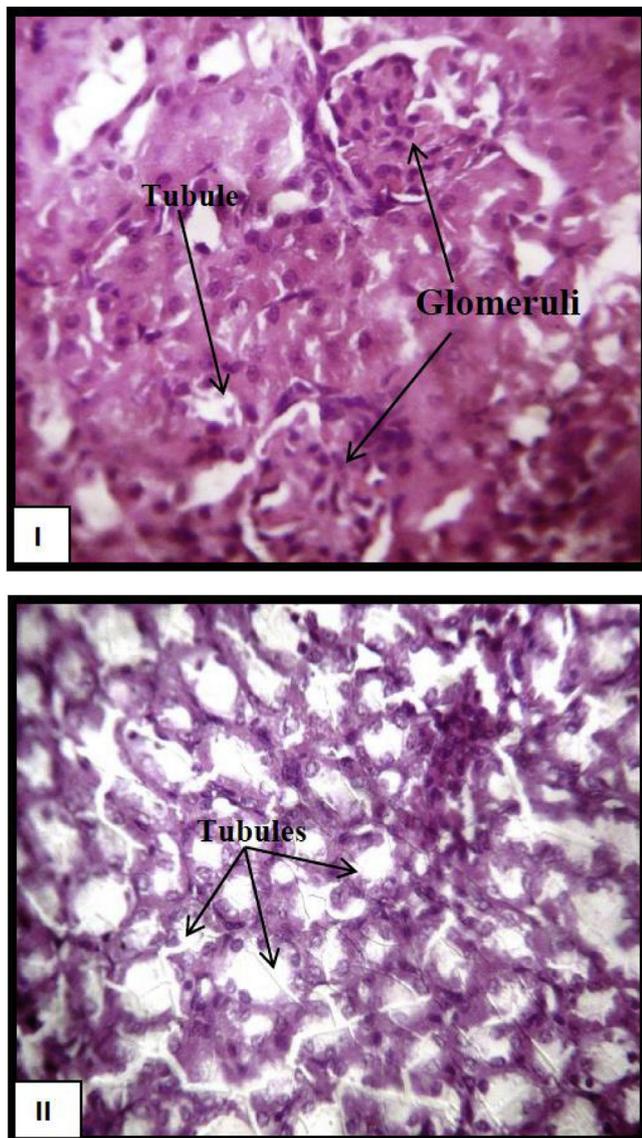


**Plate 4.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 300 mg/kg bodyweight of *Datura metel* seed extract (group 4). Marked glomerular collapse (cG) and increased urinary space (red arrow) are shown in the cortex (I); however, no obvious tissue morphological alteration of the cortical and medullary tubules is observed. (Stain: H&E; Mag: I&II-x400).

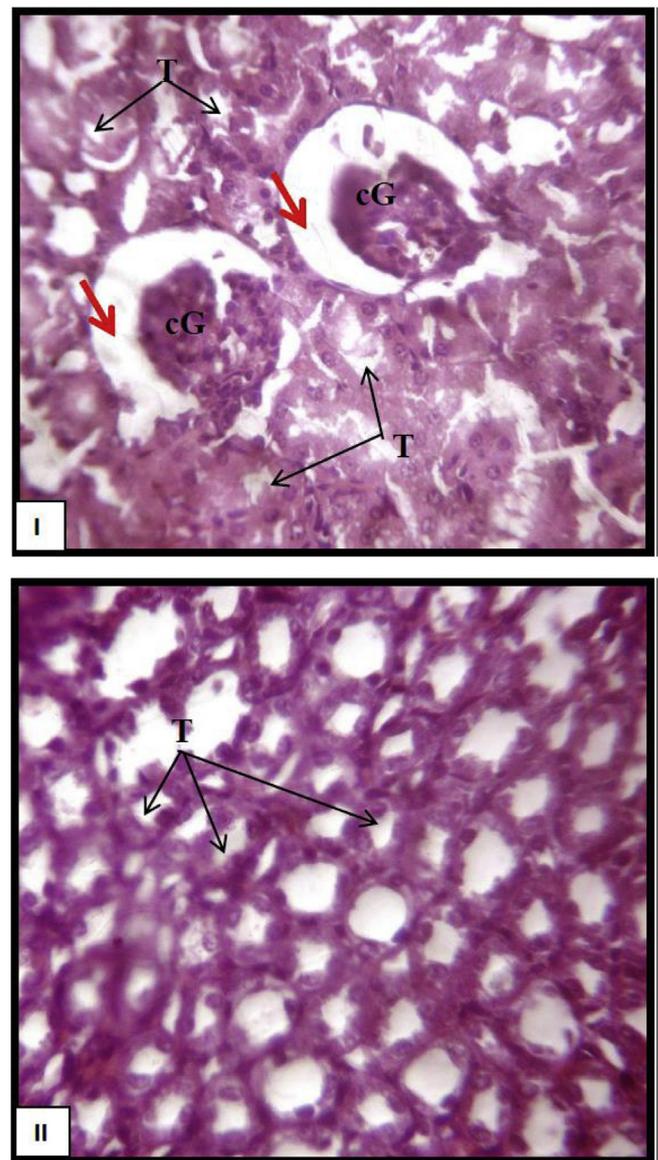
Measuring serum creatinine is a simple test, and it is the most commonly used indicator of renal function. There was significant increase in the groups administered high dose of fruit extract and low dose of seed extracts. The effect of the fruit extract was dose-dependent, while lower dose of the leaf and the seed extracts produced more effect (increased creatinine retention). Serum creatinine (a blood measurement) is an important indicator of renal health because it is an easily measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. The elevation of creatinine levels in all the groups (Table 1) show that more creatinine was retained in the blood of all the groups administered the different extracts. Nephrotoxicity is indicated by significant elevation in serum level of creatinine and urea. Creatinine retention in the blood is evidence of kidney impairment.<sup>12</sup> Creatinine is removed from the blood chiefly by the kidneys, primarily by glomerular filtration, but also by proximal tubular secretion. Little or no tubular reabsorption of creatinine occurs. A rise in blood creatinine level is observed majorly with marked

damage to functioning nephrons. The elevation of the creatinine levels in this study is believed to be as a result of the extracts administered. It is possible that the chemical constituents of the plant parts, majorly the tropane alkaloids are responsible for this negative effects.

Electrolytes (sodium, potassium, chloride and bicarbonate) balance in the blood is a good indicator of how well the kidneys and heart are functioning. Knowing which electrolytes are out of balance can help in the determination of a course of treatment. Sodium is regulated by the kidneys and adrenal glands. Sodium is the major cation of extracellular fluid. It plays a central role in the maintenance of the normal distribution of water and the osmotic pressure in the various fluid compartments. Too much sodium (hyponatremia) or too little sodium (hyponatremia) can cause cells to malfunction, and extremes in the blood sodium levels (too much or too little) can be fatal. Potassium is the principal cation of the



**Plate 5.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 600 mg/kg bodyweight of *Datura metel* seed extract (group 5). The glomeruli and tubules appear fairly intact with no obvious histomorphological alteration seen. (Stain: H&E; Mag: I & II- x400).



**Plate 6.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 300 mg/kg bodyweight of *Datura metel* fruit extract (group 6). In the cortical region, the glomeruli are collapsed resulting to increased urinary space (red arrows). However, no obvious histomorphological alteration is observed in the tubules (T) within the cortical and medullary regions. (Stain: H&E; Mag: I & II- x400).

intracellular fluid. It is also an important constituent of the extracellular fluid due to its influence on muscle activity. Elevated potassium levels (hyperkalemia) are often associated with renal failure, dehydration shock or adrenal insufficiency. Decreased potassium levels (hypokalemia) are associated with malnutrition, negative nitrogen balance, gastrointestinal fluid losses and hyperactivity of the adrenal cortex.<sup>13</sup> Chloride is important in the maintenance of the cation/anion balance between intra and extracellular fluids. This electrolyte is essential to the control of proper hydration, osmotic pressure, and acid/base equilibrium. Low serum chloride values are found with extensive burns, excessive vomiting, intestinal obstruction, nephritis, metabolic acidosis, and in Addisonian crisis. Elevated serum chloride values may be seen in dehydration, hyperventilation, congestive heart valve, and prostatic or other types of urinary obstruction.<sup>13</sup> The serum or plasma bicarbonate content is a significant indicator of electrolyte dispersion and anion deficit. Alteration of bicarbonate and CO<sub>2</sub> dissolved in plasma are characteristics of acid-base imbalance, which may be due to renal tubular acidosis, hyperkalemic acidosis, renal failure or

keto acidosis.

The concentrations of serum electrolytes measured in this study increased in all groups administered different concentrations of the extracts, except in group 4 (administered low dose: 300 mg/kg bw of seed extract), where sodium and chloride reduced non-significantly (Table 2). There was a significant increase in chloride level in group five (administered high dose: 600 mg/kg bw of seed extract) compared with normal control. Though these alterations were not statistically significant in almost all the groups administered the various extracts, but it is possible that its physiological effects could be adverse (Plate>s. 1–7). This result shows that the extracts could alter the functions of the organs associated with the electrolytes, especially the kidney (Plate>s. 1–7). Sodium, bicarbonate, chloride and potassium stability in the blood is known to be a good indicator of effective functioning of the kidneys and heart. Imo and Uhegbu (2015b)<sup>12</sup> reported that significant alteration in the concentration of these body electrolytes is indicative of poor renal functions or renal impairment.

#### 4. Conclusion

The extracts mildly altered most of the biochemical parameters used in assessing kidney function as evaluated in this study, showing its interference in kidney function. The effects of the administration of some of the extracts in comparison with the normal control on the histoarchitecture of the kidney of the animals show glomerular extrusion and collapse with resultant increased urinary space, dilated tubules, vacuolations in the epithelial lining of some of the tubules in the medulla and inflammatory cellular infiltration at some peritubular regions. The results show that some parts of *Datura metel* possess mild negative effects, while some parts (in specific concentrations) could regulate the kidney function of male albino rats. This calls for caution in the use of this plant parts and therefore suggests that the use of this plant parts should be based strictly on pharmacological need.

#### Conflicts of interest

All contributing authors declare no conflicts of interest.

#### Funding

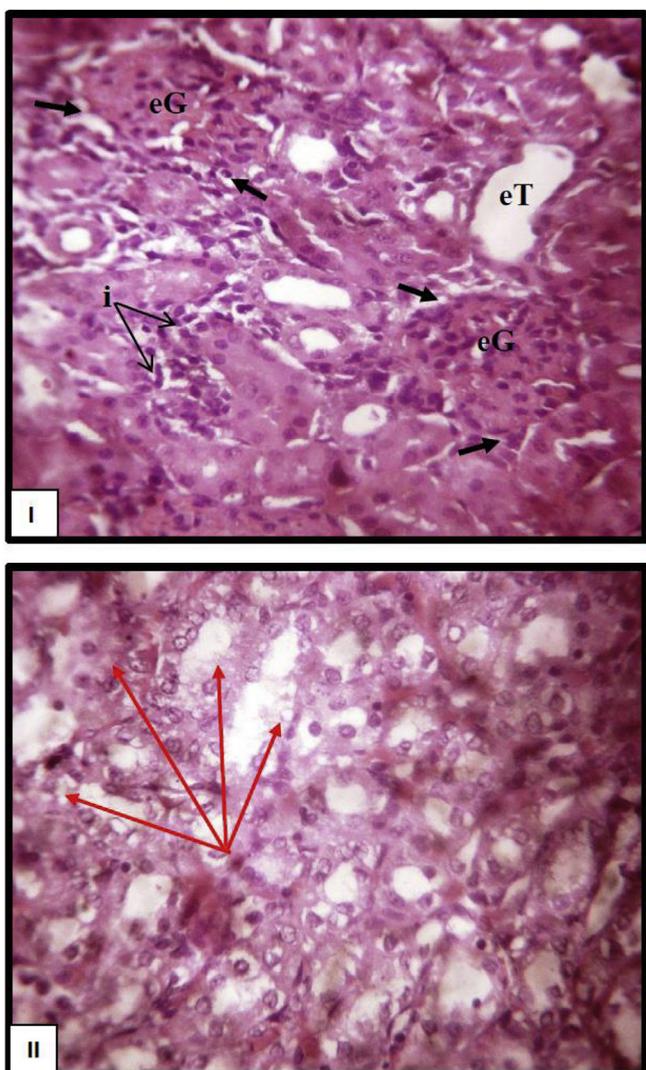
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

#### Acknowledgments

The authors appreciate the kind support of Mrs. Nkeiruka Glory Imo for her kind support, encouragement and interest in this research work. We also thank Dr. Ezekiel Iliya of the Department of Biological Sciences and Mr. Ntefreh Percy Utomobong of Biochemistry Laboratory, Federal University Wukari for their wonderful assistance during the laboratory practical of this research.

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**Plate 7.** Photomicrographs of the cortex [I] and medulla [II] of kidney section from rat administered 600 mg/kg bodyweight of *Datura metel* fruit extract (group 7). In the cortical region, the glomeruli are engorged (eG) resulting to tuft adhesion to the bowman's capsule (arrows). Inflammatory cellular infiltration is observed at peritubular regions (i) and few tubules appear eroded (eT). Note the disruption of epithelial lining of few medullary tubules (red arrows). (Stain: H&E; Mag: I& II- x400).

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