Nephrotoxicity Caused By The Extract Of Alstonia Boonei (De Wild) Stem Bark In Guinea Pigs
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Citation

Abstract
The renal effect of 50 and 200mg/kg extract of the stem bark of Alstonia boonei (De Wild) was studied in guinea-pigs of mixed sexes weighing 0.55 – 1.30kg for 2 and 4 weeks respectively. The animals were divided into six groups of 10 animals each. Groups 1 and 4 served as controls for the 2 and 4 weeks of the protocols respectively. Group 2 and 5 received 50mg/kg of the extract for 2 & 4 weeks respectively, while groups 3 and 6 received 200mg/kg of the drug product. By the 4th week, the animals in the test groups significantly lost weights (p<0.05). There was no significant difference in the weights of the kidneys (p>0.05) at the end of two weeks. 200mg/kg raised the blood urea level significantly (51.4 ± 6.12t and 31.6 ± 8.3c mg/dl) (p<0.05). Other renal parameters such as creatinine, potassium, and chloride ions were significantly raised (p<0.05) especially at 200 mg/kg dose and by the 4th week. Serum sodium and bicarbonate levels were reduced non-significantly at 50mg/kg 200mg/kg (sodium), and significantly at 50 and 200mg/kg for bicarbonate by the 4th week, relative to controls (p<0.05). The kidney cells showed obvious histological changes as a result of the administration of the extract. The plant extract may be nephrotoxic based on the results. Further studies would be needed to confirm the reproducibility of the present study.

INTRODUCTION
Alstonia boonei, a large evergreen tree belonging to the family Apocynaceae is one of the widely used medicinal plants in Africa and beyond. It is distributed throughout the tropics and the rain forest of west and Central Africa (Oliver-Bever, 1986; Olajide 2000). It is known by different names in different cultures and tribal settings. It is not edible as food but posses roots, stems, barks, leaves fruits, seeds, flowers, and latex which are claimed to have medicinal properties in some cultures an climes.

Various documented and undocumented claims have it that alcoholic or aqueous preparations from some parts of the plant especially the stem bark have medicinal uses for treating febrile illness, jaundice, painful micturition, rheumatic conditions (Ojewole, 1984; Asuzu and Onaga, 1991), as an antivenom against snake bite, as antidote against arrow poisoning etc. The extract of the stem bark is commonly used as a febrifuge in treating malaria and is listed in the African pharmacopoeia as an antimalarial drug (Olajide et al, 2000).

Various pharmacological studies have been carried out on this plant products which showed that the extracts posses antimalarial, antipyretic, analgesic and anti-inflammatory properties (Ojewole, 1984; Olajide et al, 2000), anthelmintic (Wesche et al, 1990; Wright et al, 1993), diuretic, spasmylytic and hypotensive properties (Kucera et al, 1972; Iwu 1993; Foster et al 1990), antiferile, astringent, (Iwu and Klayman, 1993), Immuno-stimulant property (Taiwo et al, 1998), antipsychotic and anxiolytic effect (Elisabetsky and Costa-campos, 2006), reversible antifertility effect. (Raji et al, 2005) among others.

In as much as many health problems have been solved using medicinal plants, a number of them are toxic if not properly prepared or properly dispensed (Dalzie, 1997). As such a scientific approach needs to be applied towards the use of plant extracts in managing ailments especially in the developing countries where the level of literacy is low and the status of health management poor, and about 80% of the population patronize herbal drugs.

The kidney is the primary organ for clearance and excretion of xenobiotics including drugs and drug-product, from the body. Damage to the kidney could arise due to the administration of plant extracts but there is paucity of scientific information because the incidence of toxicity in local settings are hardly reported nor documented. A study of the toxicity of A. boonei is imperative because of its
therapeutic and prophylactic application in many countries, especially the developing ones. Moreover, a study of the effect of the drug extract on the kidney is essential because of the cardinal role the organ plays in plasma clearance, some detoxification, homeostasis and excretion of xenobiotics. The estimation of the histological effect on the kidney tissues and the determination of some waste metabolic products excreted exclusively via the kidneys provide useful information about the health status of the kidneys; such metabolites include urea, and creatinine (Panda, 1999). Systemic electrolyte and water balance are regulated via the kidneys, thus the plasma electrolyte levels also provide vital information about the functional state of the kidneys (Nwanjo et al. 2004). The present study aims at contributing scientific knowledge regarding the possible adverse effects of A. boonei stem bark extract on renal function.

MATERIALS AND METHODS

PLANT AND ANIMALS

Preparations of stem bark extract Alstonei boonei were used for these studies. The stem bark of this plant was collected from Abob Mbaise, Imo State in the month of September, 2006 and were identified by a botanist, Dr. S. C. Okeke, of the Department of Plant Biology and Biotechnology, Imo State University, Owerri. A voucher specimen is deposited for reference in that Department.

ANIMALS

Sixty Guinea pigs of different sexes weighing between 0.55 to 1.30kg were used in the experiment. They were purchased from the Animal Science Unit of Michael Okpara University of Agriculture, Umudike, Umuahia and were transported in ventilated stainless steel cages to the Animal House of the College of Medicine and Health Sciences, Imo State University Owerri. The Guinea pigs were housed in the cages under standard conditions of temperature (25 – 29oc) and 12 hours light/dark cycle. They were maintained adlibitum on water and commercial diet (grower feed) manufactured by Guinea Farms Ltd., Ibadan, Nigeria and containing 54% carbohydrate, 10% protein, 25% fat, 20% fibre, 2% normal supplement and 1% vitamin.

The animals were left in this environment for two weeks to acclimatize. The cages were cleaned daily and water and food changed. Weights were taken after two weeks of acclimatization and the animals maintained their original weights.

EXTRACT PREPARATION

The stem bark of Alstonia boonei was collected, cut into pieces, washed and then dried in an oven (Accumax model, India) at a temperature of 50oc. The dried stem bark was then ground to a fine powder with the help of a Thomas contact mill (Pye, Unicam, Cambridge England). The powdered substance was weighed (1000g) using an electronic weighing scale (Meltter PN 163). The powder was then soaked in 24 litres of 70% ethanol using glass soxhlet extractor, stirred and allowed to stand for 24 hours. The extract was drained into amber coloured 2.5L Winchester bottles in droplets and concentrated using a rotatory evaporator (Model-Laborator 400, China). The residue in the rotatory evaporator was washed out with little ethanol and further concentrated in an oven (Accumax model, India) to constant weight. The resulting solid extract was then weighed and it gave a yield of 30.55g, representing 3.06% yield of the dry powder. A concentration of 100mg/ml of the extract was prepared for the study using normal saline.

EXPERIMENTAL DESIGN

The guinea pigs were randomly assigned to six groups of ten animals each and kept in different cages.

Group 1 served as the first control group and received 0.5ml/kg normal saline for two weeks in addition to the normal diet and water.

Group II received 50 mg/kg of the extract in addition to the normal diet and water for two weeks.

Group III received 2000 mg/kg of the extract in addition to the normal diet and water for two weeks.

Group IV served as the second control group and received 0.5ml/kg normal saline for 4 weeks in addition to the normal diet and water.

Group V received 50 mg/kg of the extract in addition to the normal diet and water for 4 weeks.

Group VI received 200 mg/kg of the extract in addition to the normal diet and water for 4 weeks. Extract was administered by oral compulsion. The weights of the guinea pigs were taken before and after the treatment.

SAMPLE COLLECTION

The animals were fasted for 24 hours after the last administration and sacrificed under chloroform anaesthesia. The blood samples were collected by cadriac puncture and
put into centrifuge tubes. The blood was allowed to clot for an hour after which it was centrifuged at 10,000 rpm for 5 minutes using Wisperfuge model 1384 centrifuge (Samson, Holland). Serum was separate with Pasteur pipette into sterile serum sample tubes and used for biochemical assay. The livers from both controls and test animals were removed and immediately washed with physiological saline and weighed.

**BIOCHEMICAL ASSAY**

Urea concentration was measured using the diacetylmonoxine method of Marchal (1957), while the creatinine concentration was determined by the alkaline picrate method (Henry et al, 1974). Serum sodium and potassium concentrations were determined using reagent titrimetrically while serum chloride concentration was determined using the mercuric nitrate method (Schaeless and Schaeless, 1941).

**STATISTICAL ANALYSIS**

Data collected were analysed using ANOVA and the students t-test (Lapin 1978). Probability value of less than or equal to 0.05 was considered significant.

**TISSUE PROCESSING**

The kidney was placed in 10% formalin for a period of 5 days for proper fixation after which the organ was cut open and smaller portions of it were selected and processed for light microscopy. The organ was dehydrated by ascending grades of isopropyl alcohol by immersing in 80% isopropanol overnight and 100% isopropyl alcohol for 1 hour. The dehydrated organs were cleared in two changes of xylene 1 hour each. The cleared organs transferred to 2 changes of liquid paraffin wax for 3 hours each using histokinette tissue processor II (Miles, USA). The wax-impregnated tissues were embedded in paraffin blocks using the same grades wax. The paraffin blocks were sectioned with Hertz Rotary microtome at 3-micron thickness. The sections were floated on a tissue flotation bath at 40°C and taken on glass slides and smeared with equal parts of egg albumin and glycerol. The sections were then melted in an incubator at 60°C for 5 minutes and allowed to cool.

**TISSUE STAINING**

The sections were deparafinised by immersing in xylene for 10 minutes in a horizontal staining jar. The deparafinised sections were washed in 100% isopropyl alcohol and stained in Ehrlich's heamatoxylin for 8 minutes in a horizontal staining jar. The sections were washed in tap water and dipped in acid alcohol to remove excess stain. The sections were then placed in running tap water or 10mins for bluing (slow alkalanization). The section were counter stained in 1% aqueous Eosin for 1minute and excess stain was washed in tap water and the sections were allowed to dry. Placing the sections in the incubator at 60oC for 5 minutes ensured complete dehydration of stained sections. When the sections were cooled, they were mouted in DPX mount having the optical index of glass (The sections were weter in Xylene and inverted on to the mount and placed on the cover slip).

**MICROSCOPY AND PHOTOMICROGRAPHY**

The sections were examined using swift® binocular microscope with in-built lighting systems. The sections were then photomicrographed using 35 minutes films with an Olympus-Photomicroscope.

**RESULTS**

Table 1 shows the changes in the mean values of the initial and final body weights of the guinea pigs treated for two weeks and four weeks respectively. The extract did not have any significant effect on the mean values of the body weights of the guinea pigs treated for two weeks (>0.05). Again no significant difference (p>0.05) was observed when the mean values of the changes in body weights of the animals treated with 50mg/kg of the extract for four weeks was compared with the control. However, a significant decrease (p<0.05) in the mean values of body weights of the guinea pigs treated with 200mg/kg extract for four weeks was observed when compared with the control.

From this analysis, it could be seen that at high dose and longer duration, the plant extract caused a significant (p<0.05) weight loss in the experimental group of guinea pigs.

Table 2 shows the mean values of the kidney weights of both the control and experimental groups of guinea pigs treated for two and four weeks respectively. There was no significant (p>0.05) increase in the kidney weight after two and four weeks.

Table 3 shows the changes in the mean values of serum urea, creatinine, sodium, pottassium, chloride and bicarbonate ions in both the control and experimental groups of guinea pigs treated for two and four weeks respectively. After two weeks no significant (p>0.05) increase in the mean values of serum urea was found at 50mg/kg dose unlike at 200mg/kg dose in which there was a significant increase in mean serum.
urea level \( (p<0.005) \) when compared with the control and within doses. But after 4 weeks, urea increased significantly \( (p<0.05) \) at both doses of 50 and 200mg/kg when compared with the control but not within doses. There was no significant \( (p>0.05) \) increase in the mean creatinine levels after two weeks at 50 and 200mg/kg doses when compared against the control and within doses.

From this analysis, it is obvious that the increase in urea and creatinine depended on the dose and duration of the extract.

Mean values of sodium showed no significant effect \( (p>0.05) \) at both 50 and 200mg/kg doses when compared with control and within doses after two weeks at the fourth weeks, mean serum sodium levels still did not significantly \( (p>0.05) \) change at 50mg/kg dose but did at 200mg/kg. This decrease in sodium ion is not clearly dose or duration dependent.

Potassium after two weeks showed no significant \( (p>0.05) \) difference in the mean serum levels at both 50 and 200mg/kg when compared with control and within doses. After four weeks, a significant \( (p<0.05) \) increases in the mean serum potassium levels was found at both doses when compared with control. This increase was dose and duration dependent. The Chloride after two weeks, showed no significant \( (p>0.05) \) increase in its mean serum levels at both doses. But after four weeks, a significant \( (p<0.05) \) increase was observed at 50 an 200mg/kg dose when compared with the control values and within doses. The increase in chloride concentration was apparently dose and duration dependent. Mean serum levels of bicarbonate showed no significant \( (p>0.05) \) change at 50 and 200mg/kg relative to control values after two weeks. But after four weeks the concentration decreased \( (p<0.05) \) relative to the control and within duration.

### Figure 1

Table 1: Changes in body weight (kg) of guinea pigs in control and the experimental groups treated for two and four weeks. (mean ± S.D. n=10)

<table>
<thead>
<tr>
<th>Duration</th>
<th>Groups</th>
<th>Initial Body Weight</th>
<th>Final Body Weight</th>
<th>Weight change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two Weeks</td>
<td>Group I (control)</td>
<td>0.82 ± 0.29</td>
<td>0.92 ± 0.23</td>
<td>0.08 ± 0.07</td>
</tr>
<tr>
<td></td>
<td>Group II (50mg/kg)</td>
<td>0.84 ± 0.11</td>
<td>0.78 ± 0.10</td>
<td>0.05 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>Group III (200mg/kg)</td>
<td>0.77 ± 0.26</td>
<td>0.65 ± 0.15</td>
<td>0.12 ± 0.05</td>
</tr>
</tbody>
</table>

| Four Weeks | Group IV (control) | 0.75 ± 0.05 | 0.9 ± 0.06 | 0.04 ± 0.02 |
|           | Group V (50mg/kg) | 0.88 ± 0.17 | 0.83 ± 0.17 | 0.03 ± 0.03 |
|           | Group VI (200mg/kg) | 0.86 ± 0.19 | 0.78 ± 0.18 | 0.08 ± 0.02* |

### Figure 2

Table 2: Mean values of organ weights (g) of both the control and experimental groups of guinea pigs treated for two weeks and four weeks. (mean ± SD) (n=10).

<table>
<thead>
<tr>
<th>Duration</th>
<th>Groups</th>
<th>Kidney weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Weeks</td>
<td>II (control)</td>
<td>4.39 ± 0.33</td>
</tr>
<tr>
<td></td>
<td>II (50mg/kg)</td>
<td>4.40 ± 0.43</td>
</tr>
<tr>
<td></td>
<td>III (200mg/kg)</td>
<td>5.49 ± 0.81</td>
</tr>
<tr>
<td>4 Weeks</td>
<td>IV (control)</td>
<td>5.10 ± 0.68</td>
</tr>
<tr>
<td></td>
<td>V (50mg/kg)</td>
<td>5.11 ± 0.12</td>
</tr>
<tr>
<td></td>
<td>VI (200mg/kg)</td>
<td>5.32 ± 0.87</td>
</tr>
</tbody>
</table>

### Figure 3

Table 3: Concentration of serum parameters (mean ± S.D) in both the control and experimental groups of guinea pigs treated for two weeks and four weeks. (n=10).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Sodium (mEq/L)</th>
<th>Potassium (mEq/L)</th>
<th>Chloride (mEq/L)</th>
<th>Bicarbonate (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Weeks</td>
<td>I (control)</td>
<td>6.6 ± 2.39</td>
<td>6.8 ± 2.27</td>
<td>132.3 ± 19.99</td>
<td>135.3 ± 20.35</td>
<td>134.5 ± 21.84</td>
</tr>
<tr>
<td></td>
<td>II (50mg/kg)</td>
<td>13.0 ± 4.36</td>
<td>16.7 ± 10.15</td>
<td>122.4 ± 15.91</td>
<td>128.6 ± 15.77</td>
<td>123.4 ± 16.61</td>
</tr>
<tr>
<td></td>
<td>III (200mg/kg)</td>
<td>31.4 ± 12.28</td>
<td>31.4 ± 10.18</td>
<td>120.8 ± 7.91</td>
<td>120.8 ± 1.17</td>
<td>120.8 ± 1.17</td>
</tr>
<tr>
<td>4 Weeks</td>
<td>IV (control)</td>
<td>34.2 ± 4.12</td>
<td>4.8 ± 0.25</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
</tr>
<tr>
<td></td>
<td>V (50mg/kg)</td>
<td>41.2 ± 2.32</td>
<td>4.8 ± 0.25</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
</tr>
<tr>
<td></td>
<td>VI (200mg/kg)</td>
<td>53.2 ± 6.45</td>
<td>6.8 ± 0.25</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
<td>138.4 ± 2.90</td>
</tr>
</tbody>
</table>

**Key:**

S.D. = Standard deviation

* = Significantly different from control \( (p<0.05) \)

** = Significantly different from control at 50mg/kg for either 2 or 4 week treatment \( (p<0.05) \).

*a = Significantly different from control and group II
(animals given 50mg/kg for two weeks) (p<0.05).
*b = Significantly different from control and group III (animal given 200mg/kg for two weeks) (p<0.5).
**b = Significantly different from control, treated animals (group v) and 200mg/kg two weeks treated animals (p<0.05).

**HISTOLOGICAL FINDINGS**

In this study 2 weeks therapy of the graded dose (50 and 200mg/kg) of the extract of A. boonei did not produce any deleterious effect on these organ examined (Fig 1-5), but produced a mild oedema, moderate hyalinization, and mild and moderate increase in the size of endothelial and mesothelia cells of the kidney in the treated guinea pigs receiving 50mg/kg and 200mg/kg respectively for 2 weeks. (Fig 2 and 3).
Results from the histological examination of the Kidney that received the lowest dose (50 mg/kg) revealed oedema, moderate vacuolation of the cytoplasm, moderate shrunken glomerulli and moderate thinckening of the basement membrane of the Bowman's capsule. (Fig 4), while the kidney that received the highest dose (200mg/kg) revealed foci necrosis, enlarged lobule, vacuolated cytoplasm, shrunken glomerular and other deleterious lesions. (Fig 5), and a dose and duration dependent shrunken glomerular in the guinea pigs treated with the extract, suggesting a decrease functional capacity of kidney.

**BIOMETRIC FINDINGS**

Table 1 shows the changes in the mean values of the initial and final body weights of guinea pigs treated for 2 and 4 weeks respectively. There was no significant effect (p>0.05) on the mean body weight changes of guinea pigs treated for 2 weeks with 50mg/kg of he extract (0.05 ± 0.02 kg and 0.11 ± 0.03 kg) respectively when compared with the control
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(0.08 ± 0.03kg). There was also no significant difference (p>0.05) in the mean values of the body weight of the animals at four weeks (0.03 ± 0.01kg) when compared with its control (0.04 ±0.02 kg). However, a significant decrease (p<0.05) in the mean values of the change in the body weights of the animals treated with 200 mg/kg of extract for 4 weeks (0.08 ± 0.03kg) was obtained when compared with the control (0.04 ±0.02kg).

Table 2 shows the mean values of the weights of Kidneys, Liver, Brain and Heart of both control and experimental groups of guinea pigs treated for 2 and 4 weeks respectively. From the results, there was no significant difference in all the organ weights in the experimental groups treated with 50 mg/kg and 200mg/kg of the extract for 2 and 4 weeks (p>0.05).

CLINICAL OBSERVATION
Clinical changes were observed in the animals receiving Alstonia boonei stem bark extract. The most consistent clinical findings were sluggishness and moderate loss of weight depending on concentration (200 mg/kg for 4 weeks) while the rest of the animals in the test group also had lost weight slightly. One animal each in groups 3 and 6 aborted spontaneously during the test period. The guinea pigs in the control group were in excellent health condition throughout the period of the study. The kidneys obtained from the control group showed no difference in their normal gross anatomical features ie. Size, colour, consistency etc but the test groups increased slightly in size.

A histopathological studies of these organ showed that 2 weeks therapy of the graded doses of the extract of Alstonia bonnie did not produce any deleterious effect on these organ. There were however a mild oedema, mild and moderate hyalinization, and mild and moderate increase in the size of endothelial and mesothelial cells of the kidney of the guinea pigs receiving 50 and 200mg/kg respectively for 2 weeks (Table3). (Fig 2-5)

Table 4 and 5 and figure 2-5 showed various lesions produced by the administration of the extract for 4 weeks. Examination of the kidney that received the highest dose (200 mg/kg) also revealed foci necrosis, enlarged lobule, vacuolated cytoplasm, shrunken glomerular and other deleterious lesions in the guinea pigs, suggesting a decreased functional capacity of the kidney (table 4) (fig 2-5).

DISCUSSION
The therapeutic importance of the extract of the stem bark of A. boonei in folk medicine have been documented (Iwu, 1993, Raji etal 2005, and Elisabesky and Costa campos, 2006). Notwithstanding, there is paucity of information regarding the adverse or toxicity of the plant extract inspite of its wide spread use in folk medicine practice. Cureenct study showed that the aqueous ethanolic extract o the stem bark could be potentially nephrotoxic, especially when the dose is high and the duration of use extended.

The administration of the extracted resulted in the functional capacity of the kidney can be measured by the dye excretion tests, concentration and dilution test as well as method for examination of blood concentration of excretory and electrolyte constituents, to demonstrate the presence or absence of active lesion in the kidney and assess the normal functioning capacity of different parts of the functioning unit-nephron (Panda, 1999). However, urea, creatinine and electrolytes (Na+, K+, HCO3- CL) are the most sensitive biochemical markers employed in the diagnosis of renal damage beause urea and creatinine are excreted through the kidney while the electrolytes are reabsorbed and excreted in the tubules. So in cellular damage, there will be retention of urea and creating in the blood and non re-absorption and non-excretion of electrolytes by the tubules (Nwanjo et al, 2005).

From table 3 however, the stem bark of Alstonia boonei was associated with consistent dose and duration dependent increase in serum urea with significant increase (p<0.05) observed in groups III,V and VI. Also creatinine showed a significant increase (p<0.05) after four weeks only at 200mg/kg dose. Urea and creatinine are waste products of protein metabolism that need to be excreted by the kidney, therefore marked increase in serum urea and creatinine are indications of functional damage to the kidney.(Panda 1999)

Although urea level can be increased by many other factors such as dehydration antidiuretic drugs diet etc. Creatinine is therefore more specific to the kidney since kidney damage is the only significant factor that increases serum creatinine level (Cheesbrough, 1998). Therefore the increase in urea and significant increase (p<0.05) in creatinine at high dose and longer duration showed that the kidney was adversely affected by the extract but the adverse effect is prominent when high dose of the extract was given for a long or period.

The final profile of Na+ concentration after four weeks in which sodium decreased significantly at 200mg/kg may be associated with the diuretic property of the plant which may have compromised the functional capacity of the nephron
especially the tubular function thereby impairing the response to aldosterone and therefore the exchange mechanisms involving re-absorption of sodium (Yakubu et al, 2005).

Potassium ions play important role in nerve impulses propagation. The Na pump maintains the intercellular K+ concentration of 140mM as against the extracellular k+ concentration of 5mM (Tiet et al, 1994). The increase in potassium observed after four weeks of extract administration was significant (p<0.05) at 50mg/kg and 200mg/kg dose relative to the control. Hyperkalaemia is a more dangerous condition because of its effect on the cardiovascular system but it rarely occurs unless renal function is depressed (Blaustein and Hamyln, 1991). It may be possible with adverse effect on the pump that maintains the constancy of the extracellular concentration (Zilva et al, 1991). However, increase in potassium observed after four weeks is an indication of reduced glomerular filtration rate of the kidney (Mayne, 1994) due to prolonged administration of extract which may have impaired potassium excretion.

Chloride increased significantly (p<0.05) at 50mg/kg and 200mg/kg doses after four weeks when compared with the control. Increase in serum chloride can be seen in dehydration renal tubular acidosis, and acute renal failure. (Nwanjo et al, 2005). The increase in chloride seen here may therefore be attributed to dehydration associated with the diuretic action of the extract which was observed in the course of the study.

For kidneys of animals treated for 2 weeks, mild oedema, hyalinization and increase in size of endothelial and mesothelial inflammation of the kidney, glomerular and pyelonephritis where observed for group 2 and 3 respectively. For guinea pigs treated for 4 weeks, the kidney showed infiltration of the glomerular tuft, enlarged lobule, vacuolated cytoplasm, oedema, glomerular degeneration and lose, possibly due to severe necrosis as Necrosis is one of the end causes of inflammatory responses (Kumar et al., 2001) given rise to possible kidney dysfunction and kidney failure for groups 5 and 6 respectively (table 3). This result may not be surprising since the kidney, s the primary organ of excretion and might have been exposed to the necrotic principle present in the extract.

It is therefore concluded that the aqueous ethanolic extract of A. boonei may be nephrotoxic especially at higher doses and on chronic application. These results portends possible dangers for patients who may be placed on long term therapy on this extract. The enlightenment of the traditional medicine practitioners on the dangers of chronic and high dose administration of the extract is imperative.

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