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Toxicity Evaluation of the Aqueous Stem Extracts of *Senna alata* in Wistar Rats

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Abstract Aim: This study evaluated the phytochemicals, proximate and the toxicity effect of aqueous stem extract of *Senna alata* using wistar rats. In acute toxicity test, aqueous dried stem extract of *Senna alata* were administered orally up to 10 g/kg body weight to male wistar rats. Materials and methods: In sub-acute study, the wistar rats were daily administered orally with aqueous dried stem extract of *Senna alata* at doses of 250, 500 and 1000 mg/kg for 14 days and haematological, biochemical parameters were determined and a histopathology of the liver and kidney were analyzed. Results: The acute toxicity of oral administration of aqueous extracts of *Senna alata* stem on albino rats after 24 hours did not produce any mortality at concentration up to 10 g/kg body weight. In the subacute toxicity, significant differences (P> 0.05) were observed in the results of urea, creatinine, and bicarbonate across the tested groups when compared with the control rats. The results of the liver enzymes showed significant difference (P> 0.05) on alkaline transaminase (ALT), Aspartate aminotransferase (AST) and Alkaline phosphatase (ALP). Conclusion: Our results showed that the dried stem of *Senna alata* is not toxic at the tested doses.

Keywords: *toxicity, biochemical, haematology, aqueous extract, wistar rats*

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1. Introduction

The quest to unravel the mysteries of bioactive properties of medicinal plants and the comprehension of their nutritional and toxicological constituents have been a subject of intense renewed interest for many scientists all over the World. Nigeria, like most developing countries is richly blessed with different herbs, shrubs, and trees. These indigenous plants have been the earliest companion of mankind, providing food, shelter and serving humanity in curing different diseases and healing of injuries [1]. The explorations of the single bioactive compounds of medicinal plants have given rise to sources of new drugs [2]. Some of these drugs have chemotherapeutic effects and are used against most life threatening diseases like cancer, AIDS, and other infectious diseases and its biological activities are studied worldwide [3,4,5]. Medicinal plants have been used from ancient time for their medicinal values of which *Senna alata* possesses.

Senna alata is a tropical perennial herb which belongs to the family, Fabaceae. It has a thick downy branched shrub and its leaflets is 8-12 pairs having the lower leaf and upper ones being oblong-elliptic and broadly obovate respectively [6]. *Senna alata* is native to Southeast Asia, Fiji, Northern Australia, Africa and Latin America [7]. This ornamental shrub grows well in forest areas of West Africa especially in aquatic environment like ponds, rivers, ditches, roadsides and drainage channels. It is commonly called Ringworm shrub and this may be likened for its use in the treatment of fungal related diseases (fungicidal and fungistatic properties) like ringworm. It is locally used in Nigeria in the treatment of several infections, which include ringworm and parasitic skin diseases [8]. It has been shown that *S. alata* possesses antibacterial, antifungal, antioxidant activities and can be used as an abortifacient [9].

The leaves, roots and stem of *Senna alata* have been reported to be useful in treating convulsion, gonorrhoea, heart failure, abdominal pains and oedema and are also used as purgative [8]. Its leaf extract is a good antioxidant and the compound obtained has been identified as a flavonol compound and named as "Kaempferol" [10,11].

The elicitation of these pharmacological actions by medicinal plants is a function of the biological chemical compounds possess by them called Phytochemicals. These bioactive compounds can be found in the different parts of the plants, the roots, stems and leaves [12]. Phytochemicals are otherwise known as Secondary plant metabolites and they have biological properties such as antioxidant activities, antimicrobial effects, modulation of detoxification enzymes, stimulation of the immune system, modulation of hormone metabolism and anticancer property. They equally help in ameliorating of diseases [13,14]. The presence of phytochemicals like phenols, tannins, saponins, alkaloids and flavonoids have been observed to give plants its antimicrobial activity [15]. The toxicological evaluation and effects of this plant have not

been properly elucidated. This work is therefore designed to bridge the gap and hence throw more light on the toxicological effects by analyzing some biochemical and haematological parameters of wistar rats fed with aqueous stem extract of *S. alata*.

2. Materials and Methods

2.1. Plant Collection and Identification

The stems of *Senna alata* were harvested fresh from bushes of Amaku Nvosi, Isiala Ngwa South Local Government Area, Abia State, Nigeria. The plant was identified and authenticated by Mr. Onyeukwu Chijioke of the Department of Plant Science and Biotechnology (Botany) University of Nigeria Nsukka. A voucher specimen (UNH/118b) was deposited in the herbarium of the Department.

2.2. Preparation of Plant Extract

The stems of *Senna alata* were washed with clean water and sun dried for 7days. After drying for seven days, they were ground into fine powder using a mechanical homogenizer. The fine powder was poured in a clean, dry container and was stored at room temperature before used for the analyses. The ground sample was soaked in distilled water (240 g in 1.5 L) for 24 h. It was filtered using a clean sieve and was concentrated to dryness in a water bath for 3 days at 50 ^{o}C. The dried extract was dispensed into airtight sterile container and stored at 4 ^{o}C in the refrigerator until usage. Extracts were later reconstituted in distilled water to give the required doses of 250, 500, 1000, 2000, 5000 and 10000 mg/kg body weight used in this study.

2.3. Phytochemical and Proximate Analysis of Stems of *Senna alata*

Phytochemical analysis of the *S. alata* stem was determined using standard analytical methods. Alkaloids, phenolics, saponins and flavonoids were quantitatively determined by the method of Harbone, [16]. Folin-Denis spectrophotometric method was employed for tannin estimation [17] and total oxalate was determined using the methods of [18].

Proximate compositions of *S. alata* stem namely; moisture, ash, crude lipid, nitrogen content, crude fibre and carbohydrate were determined according to the recommended methods of the Association of Official Analytical Chemists [19].

2.4. Laboratory Animals and Experimental Designs

Forty-five weaned male albino rats of the same stock were obtained from the animal farm of University Nigeria Nsukka. The animals were taken to the laboratory where they were housed in a wooden cage and placed on commercial feeds bought from the local market as produced by Nigeria flour mills and were allowed to drink water freely *ad libitum* till the end of the experiment, the animals weighed between 80-100g. The animals were exposed to the normal 12 h light and dark cycles under tropical weather condition. The rats were examined and allowed to acclimatize for 2 weeks prior to commencement of experiments. Ethical principles in animal handling were adhered to strictly. This study was approved by Abia State University Research, Ethics and Intellectual Development Committee with reference number (ABSU/REC/BMR/011).

2.5. Acute Toxicity Test

The rats were randomly divided into six groups of 3 animals per group. Graded oral doses of plant extracts at (250, 500, 1000, 2000, 5000 and 10000 mg/kg per oral) were separately administered orally to the rats in each group. All the rats were allowed free access to food and water and were observed for over a period of 24 h for signs of acute toxicity. The number of death, within this period was recorded.

2.6. Sub-chronic Toxicity Study

The wistar rats were randomly divided into four groups of 6 rats per group. They were fed with different concentrations of aqueous stem extract of *Senna alata* daily for 14 days. It is shown thus;

Group I: The control was given water 0.25 ml of water

Group II: They were given 250 mg/kg of aqueous stem extract of plant.

Group III: This group was administered with 500 mg/kg of the stem extracts of *Senna alata.*

Group IV: They were administered 1000 mg/kg of the aqueous stem extract of *Senna alata.*

2.7. Collection of Blood and Organ Samples

Fourteen (14) days after feeding the rats with the aqueous stem extracts of *Senna alata*, they were fasted overnight, anaesthetized with chloroform and sacrificed. Blood samples were collected by cardiac puncture using syringe and needle. Blood samples from each animal were collected into dry sample bottles for clinical chemistry analysis and EDTA (Ethylenediaminetetraacetic acid) container for hematological examination. The sample bottle with the whole blood was allowed to stand for 15 minutes to clot and further spun at 12,000 rpm for 5 minutes using the centrifuge. The Serum was separated from the clotted blood with Pasteur pipette into sterile sample test tubes for the measurement of biochemical parameters. The liver and kidney were carefully removed and placed into 10% formalin saline for histopathological analysis.

2.8. Procedures Used for Haematological and Serum Chemistry Analysis

Packed Cell Volume (PCV), Haemoglobin level (Hb), White Blood Cells count (WBC), platelets and red blood cell indices (MCV, MCHC, and MCH) were analyzed using the methods outlined by Dacie & Lewis [20].

The renal function tests; urea, creatinine, sodium, potassium, chloride and biocarbonate and liver enzymes; aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) were spectrophotometrically determined by using standard ready to use kits from Randox Laboratory Ltd, Co. Antrim, United Kingdom.

The assay kits used for total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were also products of Randox Laboratory Ltd, Co. Antrim, United Kingdom. We adhered strictly to the manufacturer's instructions for the entire biochemical test. All other reagents used were of analytical grade.

2.9. Histopathological Studies

The liver and kidney were removed carefully and fixed in 10% formalin saline in labelled sample bottles after sacrificing the rats. The tissues were processed routinely and embedded in paraffin wax. Sections of 5 µm thickness were cut and stained with haematoxylin and eosin. The processed sections were viewed using the light microscope by an experienced pathologist.

2.10 Statistical Analysis

One-way analysis of variance (ANOVA) with the R™ Statistic software package, version 3.0.3 and excel package were used for statistical analysis. The normal distribution of the data and the homogeneity of variance were tested by Bartlett homogeneity test. One-way ANOVA with a Tukey test post-hoc was used to identify statistical differences among groups. A p-value of ≤ 0.05 was considered statistically significant.

3. Results

The quantitative phytochemical estimation revealed that aqueous dried stem extract of *S. alata* contains alkaloid (1.00%), Flavonoids (6.67%), Saponin (1.33%) and oxalate, phenol and tannin, 0.75%, 033% and 0.25% respectively as shown in Table 1.

Table 1. Phytochemical composition of aqueous extract of *Cassia alata* stem

Parameters	Stem (%)
Alkaloids	1.00 ± 0.50
Flavonoids	6.67 ± 1.76
Saponins	1.33 ± 0.58
Oxalate	0.75 ± 0.14
Phenol	0.33 ±0.01
Tannin	0.25 ± 0.05

The result of the proximate analysis shows the presence of crude fibre (49.43%), carbohydrate (26.89%), crude protein (9.74%), moisture content (6.67%), ash content (5.33%) and lipid content (1.93%) as shown in Table 2.

Table 2. Proximate composition of *Cassia alata* stem

Parameter	Stem (%)
Moisture	6.67±1.52
Ash	5.33 ± 1.53
Lipid content	1.93± 0.90
Crude protein	9.74 ± 0.51
Crude fibre	49. 43 ± 0.98
Carbohydrate	26.89 ± 2.72

In acute toxicity study, no deaths were recorded in wistar rats after *S. alata stem* extracts was orally administrated at various doses ranging from 250 mg/kg to 10 g/kg body weight but scratching of body, calmness, dullness and weakness of body within 2 h were noticed among rats treated with higher doses ranging from 500 mg/kg to 10 g/kg of the post-treatment (Table 3).

Table 3. Acute (oral) toxicity study of albino rats after 24 hrs of administration of aqueous extract of *Senna alata* stem

Group	Dose (Mg/Kg)	D/T	Signs Of Toxicity
A	0.25 ml (H_2O)	0/3	No toxic effects observed
B	250	0/3	No toxic effects observed
C	500	0/3	Scratching of body and became restless within 5 minutes
D	1,000	0/3	Dullness was observed with 5 minutes
E	2,000	0/3	Scratching of body, dullness and calmness
F	5,000	0/3	Scratching of mouth and weak
G	10,000	0/3	Very weak and felt sleepy

In the sub-acute toxicity study, the percentage weight gain and relative weight of organs were not altered in all the groups (250, 500 and 1000 mg/kg body weight) treated with *S. alata* when compared to the control rats (Table 4 and Table 5).

Table 4. Effects of aqueous extract of *Senna alata* stem on the body weight of rats after 14 days administration (n=6)

Parameters	Control	250 mg/kg	500 mg/kg	1000 mg/kg
Weight at day 0	100.01 ± 9.98[a]	92.33 ± 4.12[a]	97.60 ± 5.50[a]	96.63± 7.78[a]
Weight at day 14	132.63± 12.41[a]	130.37± 1.80[a]	131.80 ± 11.25[a]	126.97± 16.66[a]
Weight gain (g)	32.62	38.06	33.20	28.34
Weight gain (%)	24.59	29.19	25.19	21.81

Values represent the mean ± SD for N=3. Values in the same row bearing the same alphabets are not significantly different from each other (P > 0.05).

Table 5. Effects of aqueous extract of *S. alata* stem on the relative organ weight of Wistar rats

Organ	Control	Group I (250 mg/kg)	Group III (500 mg/kg)	Group III (1000 mg/kg)
Liver	5.53 ± 0.08[a]	5.37 ± 0.12[a]	5.21 ± 0.70[a]	5.31 ± 0.47[a]
Spleen	0.52 ± 0.02[a]	0.45 ± 0.07[a]	0.37 ± 0.02[a]	0.41 ± 0.03[a]
Kidneys	1.22 ± 0.08[a]	1.12 ± 0.18[a]	1.96 ± 0.10[a]	1.02 ± 0.13[a]
Lung	0.84 ± 0.07[a]	1.30 ± 0.30[a]	0.88 ± 0.11[a]	1.20 ± 0.12[a]
Testes	1.54 ± 0.09[a]	1.33 ± 0.05[a]	1.32 ± 0.11[a]	0.90 ± 0.20[a]
Heart	0.47 ± 0.04[a]	0.44 ± 0.02[a]	0.37 ± 0.12[a]	0.38 ± 0.04[a]

Values represent the mean ± SD for N=3. Values in the same row bearing the same alphabets are not significantly different from each other (P > 0.05).

The results of the haematological studies as shown in Table 3.6, showed that aqueous dried stem extract of *S. alata* did not show any significant difference ($p > 0.05$) on haemoglobin, red blood cells, mean corpuscular haemoglobin, lymphocytes, neutrophil, eosinophil and mean corpuscular haemoglobin concentration in all the tested doses. However, significant difference ($p > 0.05$) was observed in the packed cell volume, white blood cell, monocytes and platelet when compared with the control group.

Table 6. Effects of aqueous extract of *S. alata* stem on haematological parameters of wistar rats

Parameters	Control	Group I (250 mg/kg)	Group II (500 mg/kg)	Group III (1000 mg/kg)
PCV (%)	41.33±1.53^{c}	37.33±1.15^{b}	34.67±3.06^{a}	38.67±1.53^{b}
Hb (g/dl)	13.76±0.51^{a}	12.47±0.40^{a}	11.56±1.04^{a}	12.88±0.50^{a}
RBC (x10^{12}/L)	6.22±0.02^{a}	5.94±0.02^{a}	4.91±0.04^{a}	6.10±0.05^{a}
MCV(fl)	66.49±2.45^{b}	62.82±2.09^{a}	70.62±5.62^{c}	63.72±2.73^{a}
MCH (pg)	22.13±0.81^{a}	21.15±0.91^{a}	23.54±1.92^{a}	21.33±0.89^{a}
MCHC (g/dl)	33.28±0.05^{a}	33.39±0.05^{a}	33.33±0.09^{a}	33.30±0.04^{a}
WBC (x 10^{9}/L)	5.27±0.31^{a}	11.70±1.05^{b}	4.70±1.61^{a}	10.51±0.36^{b}
Neutrophil (%)	46.33±2.08^{a}	46.00±0.00^{a}	44.67±2.08^{a}	50.00±1.00^{a}
Lymphocyte (%)	49.00±1.00^{a}	50.00±1.00^{a}	52.33±1.52^{a}	46.00±1.00^{a}
Eosinophil (%)	1.33±0.58^{a}	2.00±1.00^{a}	1.00±1.00^{a}	1.33±0.58^{a}
Basophil (%)	0.00±0.00	0.00±0.00	0.00±0.00	0.00± 0.00
Monocytes (%)	3.67±0.58^{b}	2.33±0.58^{a}	2.67±0.58^{a}	3.33±0.58^{b}
Platelet (x10^{9}/L)	176.67±15.28^{b}	156.67±15.28^{a}	171.67±27.54^{b}	154.33±15.04^{a}

Values represent the mean ± SD for N=3. Values in the same row bearing the same alphabets are not significantly different from each other ($P > 0.05$). PCV, Packed Cell Volume; HB, Haemoglobin; RBC, Red Blood Cells; MCV, Mean Corpuscular Volume; MCH, Mean Corpuscular Haemoglobin; MCHC, Mean Corpuscular Haemoglobin Concentration; WBC, White Blood Cell.

In the renal function test, there were statistical difference ($P > 0.05$) in the results of urea, creatinine, and bicarbonate across the tested groups when compared with the control rats. On the other there were no significant difference ($P > 0.05$) on the results of sodium ion and potassium ion. The results of the liver enzymes shows significant difference ($P > 0.05$) on alkaline transaminase (ALT), Aspartate aminotransferase (AST) and Alkaline phosphatase (ALP) as shown in Table 5.

Table 7. Effects of aqueous extracts of *Senna alata* stem on hepatic enzymes and renal function of wistar rats

Parameters	Control	Group I (250 mg/kg)	Group II (500 mg/kg)	Group III (1000 mg/kg)
Urea (mg/dl)	40.02 ± 0.19^{b}	39.20 ± 1.09^{b}	34.90 ± 1.84^{a}	34.58 ± 1.23^{a}
Creatinine (mg/dl)	1.67 ± 0.09^{b}	0.94 ± 0.03^{a}	1.64 ± 0.13^{b}	1.59 ± 0.10^{b}
Na^{+} (mEq/L)	140.59 ± 0.70^{a}	137.22 ± 3.90^{a}	137.53 ± 1.26^{a}	139 ± 3.79^{a}
Cl^{-} (mEq/L)	104.61 ± 1.26^{c}	97.72 ± 1.32^{a}	98.28 ± 0.95^{a}	101.27 ± 1.11^{b}
K^{+} (mEq/L)	5.06 ± 0.07^{a}	5.23 ± 0.11^{a}	5.22 ± 0.14^{a}	4.75 ± 0.22^{a}
HCO_3^{-} (mMol/L)	29.18 ± 0.75^{b}	25.67 ± 0.61^{bc}	27.42 ± 0.23^{b}	23.49 ± 0.78^{a}
ALT (U/L)	8.43±0.56^{a}	17.43±0.89^{b}	7.28±0.25^{a}	8.49±0.32^{a}
AST (U/L)	18.38±0.82^{b}	13.15±0.44^{a}	14.76±3.18^{a}	12.28±0.75^{a}
ALP (U/L)	44.47±1.85^{a}	42.81±2.40^{a}	58.78±1.17^{b}	45.44±6.41^{a}

Values represent the mean ± SD for N=3. Values in the same row bearing the same alphabets are not significantly different from each other ($P > 0.05$). Na^{+}, Sodium ion; Cl^{-}, Chloride ion; K^{+}, Potassium ion; HCO_3^{-}, Biocarbonate; ALT, Alanine Transaminase; AST, Aspartate Aminotransferase; ALP, Alkaline Phosphatase.

The results of the lipid profile (Table 8) showed slightly decrease in total cholesterol and LDL-C when compared with the control rats. A slight increase in the HDL-C was observed across the groups when compared to the control. The group treated with 500mg/kg body weight had the highest values in triglycerides (148.29 mg/dl) and very low-density lipoprotein cholesterol (29.66 mg/dl) when compared to the other doses as well as the control. Interestingly all the tested parameters in this study were within the standard normal reference range for each parameter.

Table 8. Effects of aqueous stem extract of *Senna alata* on lipid profile of wistar rats

Parameters	Control	Group I (250 mg/kg)	Group II (500 mg/kg)	Group III (1000 mg/kg)
Total cholesterol(mg/dl)	120.91±2.68^{b}	113.17±9.63^{b}	95.70±2.47^{a}	101.16±1.37^{a}
Triglycerides (mg/dl)	126.47±4.99^{a}	119.61±9.28^{a}	148.29±11.63^{b}	121.22±11.73^{a}
HDL-C (mg/dl)	42.89±0.57^{a}	45.06±0.60^{a}	44.16±0.35^{a}	43.72±0.58^{a}
LDL-C (mg/dl)	45.02±10.92^{c}	41.09±13.68^{c}	24.95±7.48^{a}	31.90±3.49^{b}
VLDL-C (mg/dl)	25.30±1.00^{a}	22.15±3.13^{a}	29.66±2.32^{b}	24.24±2.34^{a}

Values represent the mean ± SD for N=3. Values in the same row bearing the same alphabets are not significantly different from each other ($P > 0.05$). HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol; VLDL-C, Very Low-Density Lipoprotein Cholesterol.

Figure 1 below shows the histopathological examination of the liver of the wistar rat treated with doses of 250mg/kg, 500mg/kg and 1000mg/kg did not reveal any pathological changes when compared to the control rats.

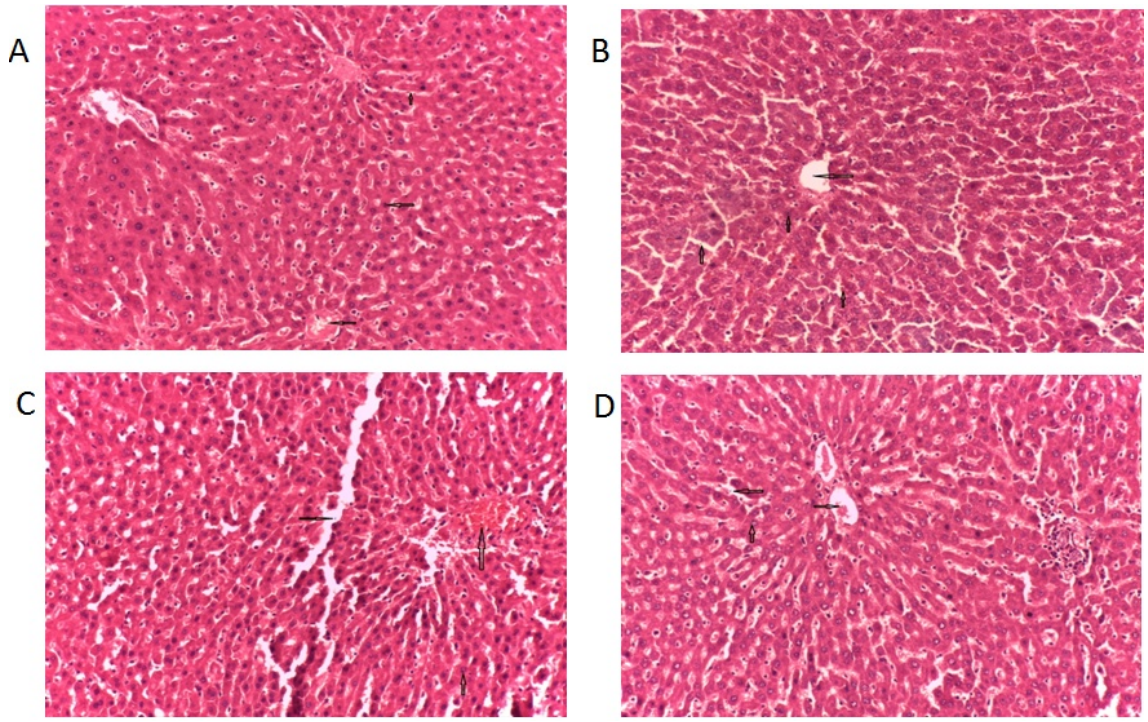

Figure 1. Micrographs of the liver sections obtained from untreated (control) and treated wistar rats with various doses of aqueous dried stem extract of *Senna alata*. Haematoxylin and eosin staining (H&E), Magnification (40×). (A), control (B), wistar rats treated with 250 mg/kg stem extract of *Senna alata*. (C), wistar rats treated with 500 mg/kg stem extract of *Senna alata*. (D), wistar rats treated with 1000 mg/kg stem extract of *Senna alata*

Figure 2 below shows the histopathological examination of the kidney of the wistar rat treated with doses of 250mg/kg, 500mg/kg and 1000mg/kg did not reveal any pathological changes when compared to the control rats.

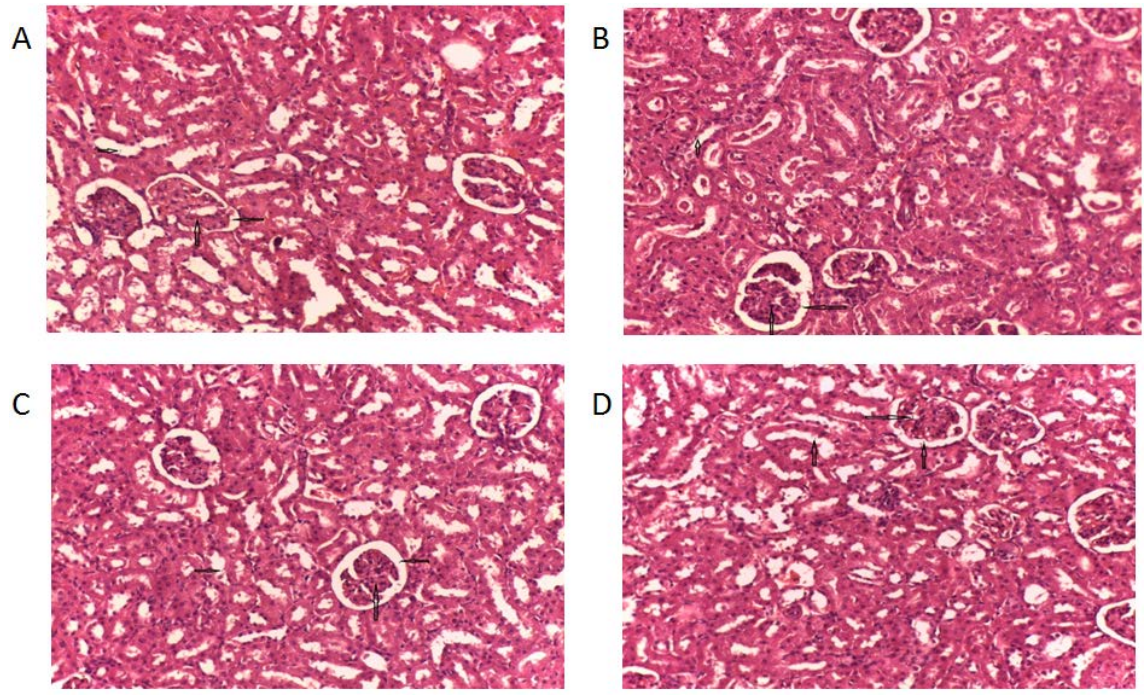

Figure 2. Micrographs of the kidney sections obtained from untreated (control) and treated wistar rats with various doses of aqueous dried stem extract of *Senna alata*. Haematoxylin and eosin staining (H&E), Magnification (40×). (A), control (B), wistar rats treated with 250 mg/kg stem extract of *Senna alata*. (C), wistar rats treated with 500 mg/kg stem extract of *Senna alata*. (D), wistar rats treated with 1000 mg/kg stem extract of *Senna alata*

4. Discussion

The health benefits of medicinal plants cannot be overemphasized. The bioactive compositions of medicinal plants have given rise to the treatment of various diseases and production of new drugs. Thus, their individual concentration should be taken into account for the necessity of their toxicological studies. This present study, therefore evaluated the nutritional constituents, pharmacological actions and toxicological assessment of aqueous stem extract of *Senna alata* in wistar rats by quantifying their proximate, selected phytochemical, biochemical and haematological parameters.

The quantitative phytochemical estimation revealed that aqueous dried stem extract of *S. alata* contains alkaloid, which is one of the most efficient therapeutic bioactive compounds in plants because of its analgesic and bactericidal effects [21]. Alkaloids are also known to exhibit marked physiological activity when administered to animals. Pure isolated plant alkaloids and their synthetic derivatives are used as basic medicinal agents for pain relieving, anti-plasmodic and bactericidal effects [22,23].

Saponin was 1.33% and can be considered as safe and non-toxic [24]. Saponins are useful in medicine and pharmaceutical industry due to their foaming ability that produces frothing effects. Flavonoids have the highest composition (6.83%), indicating that *S. alata* can help fight against microbes and hepatic toxicity [25]. It has also been reported that flavonoids possess greater benefit to human health, antimicrobial, cytotoxicity, anti-tumor and anti-inflammatory activities [26] and it is also known for its unique intestinal tract function which aids in lowering the risk of heart diseases [27]. Flavonoids are good antioxidants and free radical scavengers which prevent oxidative cell damage, have strong anticancer and protect cell against all stages of carcinogenesis [27,28]. The result shows that the stem of *S. alata* consists of phenols (0.33%), tannins (0.25%) and oxalate (0.75%). Phenols and phenolic compounds are extensively used as disinfectant and remain the standard with which other bactericides are compared. The presence of these phytochemicals in *S. alata* supports its use in herbal medicine and can be a rich source of food and drug [29].

The results of the proximate composition showed the presence of high crude fibre (49.43%) which is a good indication that the plant can prevent diverticulosis and also aid in the absorption of trace elements in the guts [30]. This shows the efficiency of the extract in gastrointestinal motility and fermentation in the large intestine by inherent bacterial flora and also may not be metabolized by bacteria in the large intestine as seen in insoluble fibers. Carbohydrate (26.89%), which can serve as energy source while moisture content and ash content fell within the range of acceptable limits (6-15%) for most vegetables [24]. Protein value is 9.74%. Proteins help in the building of new cells and replacing of old ones. They are also essential for formation of enzymes and hormones. Protein energy malnutrition or its deficiency in the body leads to kwashiorkor, reduced intelligence or mental retardation [31].

Toxicity has been an expression of being poisonous, indicating the state of adverse effects led by the interaction between toxicants and cells [32]. The acute toxicological investigation (LD_{50}) of the aqueous stem extract of *Senna alata* showed no mortality at the maximum dose of 10g/kg per body weight after 24 h administration of the extract, although the wistar rats administered at this concentration felt weak and sleepy. Therefore, according to Lorke [33], the plant in its local formulation can be categorized as non-toxic.

In the sub-acute toxicity study, the wistar rats were orally administered daily with various doses of aqueous extract of *S. alata* at 250, 500 and 1000 mg/kg body weight. The animals gained weight after 14 days of administration. This increase in body weight could be attributed to the nutritional compositions present in the feed and aqueous stem extract [34]. The estimated relative organ weights were not altered when compared to the control ($p< 0.05$). It has been shown that loss or gain in these organ weights is a sensitive tool in toxicological study [35]. This stability in the organ weight is an indication that the aqueous stem extract of *S. alata* did not have a negative effect on the organs.

This study alsodemonstrated a marked level in the haematological parameters within the reference range and this suggested that the aqueous stem extract of *S. alata* did not affect the blood producing organ, bone marrow, which has been an indicator and targeted organ of toxicants [36]. Conventional drugs or chemicals affect adversely the various blood components [37]. Haematotoxicity sets in when there is alteration in these blood components beyond their reference ranges [35].

It has been reported that some herbal mixtures have hepatotoxic and nephrotoxic effects [38,39]. The loss of integrity and functionality of these homeostatic organs (liver and kidney) would certainly lead to the increase of clinical chemistry parameters like serum enzymes and analytes. Serum enzymes like AST, ALT and ALP and analytes like urea, creatinine and electrolytes like Na^+, K^+, Cl^- and HCO_3^- [40]. A marked level of the hepatic enzymes (AST, ALT and ALP) and the analytes within the reference range which are markers of cellular damage post 14 days oral administration of the aqueous stem extract of *S. alata* at the tested doses were observed in the course of the study with no effect when compared to the control ($p< 0.05$).

The current study also showed a normal effect on lipid profile, LDL-C (Low density lipoprotein), HDL-C (High density lipoprotein), VLDL-C (Very low density lipoprotein), TG (Triglycerides) and TC (Total cholesterol) in the groups fed with different concentrations of the stem extract within their serum ranges. Antagonisto-hyperlipidemic effects of this extract may be due to the down regulation of Nicoatinamide adenine dinucleotide phosphate (NADPH) and Nicoatinamide adenine dinucleotide (NADH) cofactors in the fat metabolism and that of oxidizing NADPH. The maintenance reference serum level suggests the extract has beneficial activity to the liver [41].

In toxicological studies, histopathological analysis provides cogent evidence for biochemical and haematological observations [42]. The results showed normal architectural design and integrity of the liver and kidney of the different groups administered different concentrations of the aqueous stem extract of *S. alata*.

5. Conclusions

This study shows that the stem of *Senna alata* is not toxic at the tested doses.

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