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Toxicological assessment of the aqueous dried leaf extracts of *Senna alata* L. in wistar rats

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Senna alata **is a medicinal plant that belongs to Leguminosae family. Different parts of the plant are used in folklore medicine for curing skin infections, abdominal pain, and gonorrhoea. Despite the use of *S. alata* in the treatment of various ailments, there is limited or no comprehensive scientific information on the toxicological evaluation of the dried leaf extract in the folklore medicine in Africa. This study therefore evaluated the extensive toxicological effects of the aqueous dried leaf extract of *S. alata* in wistar rats. In acute toxicity test, aqueous dried leaf extract of *S. alata* were administered orally up to 10 g/kg body weight to male wistar rats. In sub-acute study, the wistar rats were daily administered orally with aqueous dried leaf extract of *S. alata* at doses of 250, 500 and 1000 mg/kg for 14 days and haematological and biochemical parameters were determined and a histopathology of the liver and kidney were analysed. The results revealed that in acute toxicity study, no death was recorded within 24 h after oral administration. In the sub-acute study, the extract did not exhibit any significant difference ($p > 0.05$) on haemoglobin, red blood cells and mean corpuscular haemoglobin concentration in all the tested doses. Significant differences ($p > 0.05$) were observed on white blood cell, platelet, urea, aspartate aminotransferase, alkaline phosphatase, total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. The histopathology of the liver and kidney did not reveal any pathological changes. Our findings revealed that aqueous dried leaf extract of *S. alata* is not toxic at the tested doses, indicating that it is safe for therapeutic uses at the tested doses.**

Key words: Haematology, hepatic and renal function, sub-acute toxicity, histopathology, *Senna alata*.

INTRODUCTION

The practice of herbal medicine is as old as the origin of mankind (Petrovska, 2012). Today, the use of plant-based herbal remedies is spreading worldwide and is gradually gaining general acceptance, because it is used in both the developing countries as the major primary health care of the poor and also in developed countries where modern medicine is dominant in the national health care system (Tahvilian et al., 2014). For example, the use of quinine and quinidine extracted from *Cinchona* tree and also artemisinin obtained from

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Artemisia annuain for treating malaria is an indication that medicinal plants are essential sources of novel drugs (Igoli et al., 2005).

Herbal medicine plays vital role as hypolipidemic (Yadav et al., 2008), abortifacient and contraceptive (Yakubu et al., 2010), antihypertensive (Nworgu et al., 2008), effective for treating skin diseases (Ajibesin et al., 2008), wound healers, and hypoglycemic effects and antimicrobial activities (Lee et al., 2009). Herbal medicine has numerous advantages such as low-cost, affordability, availability, accessibility, acceptability, and low toxicity; however, there are various disadvantages of consuming herbal products which include inappropriate formulations, lack of adequate scientific proof of the plant, imprecise diagnosis dosage and unstandardized usage which can lead to serious health risk to the patients (Elujoba et al., 2005).

Senna alata (L.) Roxb. is a medicinal plant that belongs to Leguminosae family. It is an important ornamental flowering plant commonly known as candle tree, ringworm plant and candle bush (Singh et al., 2012; Otto et al., 2014) and exist in diverse environments like ditches, rivers, margins of ponds, drainage channels and alongside water ways in Africa. In traditional medicine, the leaves, roots and stems are widely used for treatment of skin infections (Lifongo et al., 2014), abdominal pain (Hennebelle et al., 2009), gonorrhoea and heart failure (Otto et al., 2014). It is used as anti-bacterial, laxative, diuretic, treatment of flu, malaria and other infectious diseases (Hennebelle et al., 2009). It has been reported that *S. alata* leaves possess antimutagenic (Villaseñor et al., 2002), anti-inflammatory, and antimicrobial properties (Khan et al., 2001; Somchit et al., 2003).

Previous studies on *S. alata* have shown that it possesses antifungal (Palanichamy and Nagarajan, 1990), anti-bacterial activities (Somchit et al., 2003), antioxidant properties (Sagnia et al., 2014) and can be used as abortifacient (Yakubu et al., 2010). Hennebelle et al. (2009) also reported the laxative and purgative potentials of *S. alata*, but to the best of our knowledge there is limited or no comprehensive scientific documentation on the toxicological evaluation of the leaf extract of *S. alata* in the folklore medicine. Therefore, this present study is aimed at evaluating extensively the toxicological effects of the leaf extract of *S. alata* in wistar rats.

MATERIALS AND METHODS

Plant collection and authentication

Fresh leaves of *S. alata* were collected from Amaku Nvosi in Isiala Ngwa South Local Government Area of Abia State, Nigeria in July, 2015 (Figure 1). 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.

Preparation of plant extract

Fresh leaves of *S. alata* were destalked and washed with deionized water before sun drying for 7 days. The dried leaves were milled into fine powder and then macerated in sterile distilled water (300 g in 2 L) for 24 h. The extract was decanted and filtered with Whatman filter paper No. 1 and the filtrate was concentrated to dryness in a water bath for 3 days at 50°C giving a greenish brown colour. The dried extract was dispensed into airtight sterile container and stored at 4°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.

Phytochemical and proximate analysis of leaves of *S. alata*

Phytochemical analysis of the *S. alata* leaf was determined using standard analytical methods. Alkaloids, phenolics, saponins, and flavonoids were quantitatively determined by the method of Harborne (1973). Tannin was determined using the Folin-Denis spectrophotometric method (Shabbir et al., 2013) and total oxalate was estimated according to the methods of Day and Underwood (1986).

The proximate compositions of *S. alata* leaf, 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 (AOAC, 2005).

Animals

Forty-five (45) healthy male albino rats (80 to 100 g) used in this study were purchased from animal house of University of Nigeria, Nsukka, Enugu State, Nigeria. The rats were transported to Department of Biochemistry, Abia State University, Uturu, Abia State, Nigeria. The albino rats were kept under normal standard environmental conditions of humidity (35 to 60%), temperature (25 to 28°C) and a 12 h/12 h light/darkness cycle and were fed *ad libitum* with standard feed and allowed free access to water. The albino rats were allowed to acclimatize to laboratory conditions for two weeks before the commencement of the study. The albino rats were handled in accordance with the World Health Organization (WHO) good laboratory practice regulations of 1998 and United State guidelines for experimental animal (NIH publication #85-23, revised 1996). Ethical principles in animal care and handling were strictly adhered throughout the study (Neuwinger, 2000).

Acute toxicity test

The rats were randomly divided into 7 groups of 3 animals per group. Graded oral doses of plant extract (250, 500, 1000, 2000, 5000, and 10000 mg/kg) were separately administered orally to the rats in each group. The control group was orally given 0.25 ml of distilled water. All the rats were allowed free access to food and water and were observed for a period of 24 h post-treatment for behavioural changes, signs of toxicity, and mortality.

Sub-chronic toxicity study

The albino rats were randomly divided into 4 groups of 6 rats per group. The rats were orally administered *ad libitum* an aqueous dried leaf extract of *S. alata* at doses of 250, 500, and 1000 mg/kg daily for 14 days. The control group was orally administered 0.25 ml of distilled water daily. The rats were weighed daily throughout the course of the experiment.

Figure 1. The leaves of *Senna alata*.

Collection of blood and organ samples

Fourteen days after feeding the rats with the aqueous dried leaf extracts of *S. alata*, they were fasted overnight, anaesthetized with chloroform and sacrificed. Blood samples were collected through cardiac puncture with the help of syringe and needle and dispensed into ethylenediaminetetraacetic acid (EDTA) containers for haematological analysis and heparinized containers for blood chemistry test.

The organs, namely, liver, kidneys, heart, lungs, spleen, and testes were dissected and removed carefully and absolute weights of each organ were determined. The relative organ weight of individual wistar rats was calculated as follows:

Relative organ weight = (Absolute organ weight (g) / Body weight of rat on sacrificed day (g)) × 100

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 (mean corpuscular volume [MCV]; mean corpuscular haemoglobin [MCH]; mean corpuscular haemoglobin concentration [MCHC]) were analyzed using the methods outlined by Dacie and Lewis (1991).

The renal function tests; urea, creatinine, sodium, potassium, chloride and bicarbonate and liver enzymes; alanine aminotransferase (ALT), aspartate aminotransferase (AST), and 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. The manufacturer's instructions for the entire biochemical test were strictly adhered to.

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

Table 1. Phytochemical constituents of aqueous dried leaf extract of *S. alata*.

Parameter	Leaves
Alkaloids	3.17 ± 0.29
Flavonoids	1.53 ± 0.76
Saponins	2.83 ± 0.29
Oxalate	1.37 ± 0.03
Phenol	0.87 ± 0.01
Tannin	0.82 ± 0.15

Values represent the mean ± SD for N=3.

Table 2. Proximate composition of dried leaf of *S. alata*.

Parameter	Leaves (% w/w)
Moisture content	7.33 ± 1.53
Ash content	7.33 ± 1.53
Lipid content	3.27 ± 0.23
Crude protein	11.20 ± 0.31
Crude fibre	53. 87 ± 0.98
Carbohydrate	17.00 ± 3.87

Values represent the mean ± SD for N=3.

Table 3. Acute (oral) toxicity study of albino rats after 24 h of administration of aqueous dried leaf extract of *S. alata*.

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 2 min
D	1,000	0/3	Dullness was observed with 5 min
E	2,000	0/3	Scratching of body, dullness and calmness
F	5,000	0/3	Scratching of mouth and weakness
G	10,000	0/3	Very weak and felt sleepy within 2 h

D/T: Number of albino rat deaths/Total number of albino rats used.

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.

Statistical analysis

One-way analysis of variance (ANOVA) with the R^{TM} 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.

RESULTS

The quantitative phytochemical estimation revealed that aqueous dried leaf extract of *S. alata* contains alkaloid (3.17%), followed by saponin (2.83%), flavonoids (1.53%), oxalate (1.37%), phenol (0.87%), and tannin (0.82%) are shown in Table 1. The result of the proximate analysis shows the presence of crude fibre (53.87%), carbohydrate (17.00%), crude protein (11.20%), moisture content (7.33%), ash content (7.33%), and lipid content (3.27%) are shown in Table 2.

In acute toxicity study, no deaths were recorded in wistar rats after *S. alata* extracts were orally administrated at various doses ranging from 250 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 to 10 g/kg of the post-treatment (Table 3).

In the sub-acute toxicity study, the percentage weight

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

Parameter	Control	250 mg/kg	500 mg/kg	1000 mg/kg
Weight at day 0	100.01 ± 9.98^{b}	83.87 ± 6.26^{a}	94.00±2.76^{b}	87.50±9.87^{a}
Weight at day 14	132.63 ± 12.41^{c}	109.73±2.21^{a}	117.97±3.09^{b}	110.70±24.42^{a}
Weight gain (g)	32.62	25.86	23.97	23.20
Weight gain (%)	24.59	23.57	20.32	20.96

Values represent the mean ± SD for N=6. Values in the same row bearing the same alphabets are not significantly different from each other (P > 0.05).

Table 5. Effect of aqueous dried leaf extract of *S. alata* on the relative organ weight of wistar rats.

Organ	Relative organ weight (g) of albino rats			
	Control	Group I (250 mg/kg)	Group II (500 mg/kg)	Group III (1000 mg/kg)
Liver	5.53 ± 0.08^{a}	4.67 ± 0.43^{a}	4.51 ± 0.43^{a}	4.48 ± 1.07^{a}
Spleen	0.52 ± 0.02^{a}	0.31 ± 0.09^{a}	0.36 ± 0.04^{a}	0.34 ± 0.03^{a}
Kidneys	2.44 ± 0.08^{a}	1.86 ± 0.05^{a}	1.80 ± 0.01^{a}	1.78 ± 0.11^{a}
Lungs	0.84 ± 0.07^{a}	0.86 ± 0.09^{a}	0.87 ± 0.09^{a}	0.89 ± 0.32^{a}
Testes	3.08 ± 0.09^{a}	2.00 ± 0.11^{a}	1.96 ± 0.30^{a}	2.58 ± 0.30^{a}
Heart	0.47 ± 0.04^{a}	0.34 ± 0.03^{a}	0.38 ± 0.04^{a}	0.34 ± 0.05^{a}

Values represent the mean ± SD for N=6. Values in the same row bearing the same alphabets are not significantly different from each other (P > 0.05).

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

Parameter	Control	Group I (250 mg/kg)	Group II (500 mg/kg)	Group III (1000 mg/kg)
PCV (%)	41.33±1.53^{c}	38.00± 2.00^{bc}	33.33±1.53^{a}	35.33±3.51^{ab}
Hb (g/dl)	13.76±0.51^{a}	12.66±0.65^{a}	11.12±0.50^{a}	11.88±1.32^{a}
RBC (×10^{12}/L)	6.22±0.02^{a}	5.74±0.02^{a}	4.77± 0.15^{a}	5.84±0.02^{a}
MCV(fl)	66.49±2.45^{b}	66.21±3.72^{b}	69.28±2.24^{c}	60.52±6.22^{a}
MCH (pg)	22.13±0.81^{a}	22.05±1.21^{a}	23.38±1.72^{a}	20.18±2.07^{a}
MCHC (g/dl)	33.28±0.05^{a}	33.31±0.05^{a}	33.37±0.06^{a}	32.33±1.75^{a}
WBC (× 10^{9}/L)	5.27±0.31^{bc}	6.97±0.25^{c}	4.73±0.97^{ab}	4.13±0.32^{a}
Neutrophil (%)	46.33±2.08^{a}	45.67±0.58^{a}	46.67±1.15^{a}	46.00±1.00^{a}
Lymphocyte (%)	49.00±1.00^{a}	49.00±2.00^{a}	49.33±1.15^{a}	50.00±2.65^{a}
Eosinophil (%)	1.33±0.58^{a}	1.33±0.58^{a}	1.33±0.58^{a}	1.67±1.15^{a}
Basophil (%)	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
Monocytes (%)	3.67±0.58^{b}	3.00±1.00^{ab}	2.67±1.15^{ab}	2.33±1.58^{a}
Platelet (×10^{9}/L)	176.67±15.28^{c}	153.33±20.82^{a}	153.33±7.64^{a}	163.33±15.28^{b}

Values represent the mean ± SD for N=6. 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.

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 with the control rats (Tables 4 and 5).

The results of the haematological studies as shown in Table 6, showed that aqueous dried leaf 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 white blood cell, mean corpuscular volume, packed cell volume, monocytes and platelet when compared with the control rats.

Table 7. Effects of aqueous dried leaf extract of *S. alata* on hepatic enzymes and renal function of wistar rats.

Parameter	Control	Group I (250mg/kg)	Group II (500mg/kg)	Group III (1000 mg/kg)
Urea (mg/dl)	40.02 ± 0.19^{b}	37.38 ± 0.71^{ab}	34.74 ± 1.28^{a}	34.58± 1.17^{a}
Creatinine (mg/dl)	1.67 ± 0.09^{b}	0.81 ± 0.08^{a}	1.23± 0.07^{b}	1.30 ± 0.10^{b}
Na^+ (mEq/L)	140.59 ± 0.70^{a}	136.13 ± 4.47^{a}	138.55 ± 3.75^{a}	137.04 ± 2.76^{a}
Cl^- (mEq/L)	104.61 ± 1.26^{c}	101.92 ± 0.34^{b}	98.71 ± 0.50^{a}	98.11 ± 0.82^{a}
K^+ (mEq/L)	5.06 ± 0.07^{b}	5.11 ± 0.07^{b}	4.20 ± 0.09^{a}	4.26 ± 0.59^{a}
HCO_3^- (mMol/L)	29.18 ± 0.75^{c}	27.73 ± 0.50^{b}	27.83 ± 0.63^{b}	22.33 ± 1.96^{a}
ALT (U/L)	8.43 ± 0.56^{a}	12.74 ± 2.34^{a}	7.68 ± 0.42^{a}	9.99 ± 0.64^{a}
AST (U/L)	18.38 ± 0.82^{b}	9.33 ± 2.08^{a}	15.49 ± 3.75^{b}	18.16 ± 1.18^{b}
ALP (U/L)	44.47 ± 1.85^{b}	57.20 ± 1.66^{c}	38.15 ± 1.38^{a}	61.28 ± 4.67^{c}

Values represent the mean ± SD for N=6. 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^-: bicarbonate; ALT: alanine transaminase; AST: aspartate aminotransferase; ALP: alkaline phosphatase.

Table 8. Effects of aqueous dried leaf extract of *S. alata* on lipid profile of wistar rats.

Parameter	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}	122.34±2.05^{b}	105.26±10.29^{a}	115.75±7.84^{b}
Triglycerides (mg/dl)	126.47±4.99^{a}	145.50±5.07^{b}	121.10±10.67^{a}	127.87±5.00^{a}
HDL-C (mg/dl)	42.89±0.57^{a}	43.67±0.11^{a}	43.18±0.87^{a}	43.78±1.04^{a}
LDL-C (mg/dl)	45.02±10.92^{c}	46.62±5.91^{c}	37.57±8.43^{a}	43.19±8.70^{b}
VLDL-C (mg/dl)	25.30±1.00^{a}	29.10±1.00^{b}	24.22±2.14^{a}	25.57±1.00^{a}

Values represent the mean ± SD for N=6. 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.

In the renal function test, a slight decrease in the results of urea, creatinine, sodium ion, potassium ion, and bicarbonate was observed across the tested groups when compared with the control rats. On the liver enzymes parameters, there was no significant difference (P>0.05) on ALT. AST decreases when administered the dried leaf aqueous extract of *S. alata* at 250 and 500 mg/kg to 9.33 and 15.49 U/L, respectively, and increased to 18.16 U/L at 1000 mg/kg body weight, while the control had 18.38 U/L. ALP showed statistical significance (P> 0.05) with values of 44.44, 57.20, 38.15 and 61.28 U/L for the control, 250, 500 and 1000 mg/kg doses of the extract, respectively (Table 7).

The results of the lipid profile (Table 8) showed slightly higher values at 250 mg/kg dose for total cholesterol (122.34 mg/dl), triglycerides (145.5 mg/dl), low-density lipoprotein cholesterol (46.62 mg/dl), and very low-density lipoprotein cholesterol (29.10 mg/dl) when compared with the other doses as well as the control. The histopathological examination of the liver (Figure 2) and kidney (Figure 3) of the wistar rats in all the treated doses of the aqueous dried leaf extract of *S. alata* did not reveal any damage or pathological changes when compared with the control rats.

DISCUSSION

Despite the tremendous use of medicinal plants in treatment of various ailments in Africa and other parts of the world, there are still few documented scientific studies on toxicological evaluation of medicinal plants to ascertain the efficacy and safety usage of herbal remedies for human consumption. This present study, therefore evaluated the selected phytochemicals, proximate compositions, and toxicological effects of aqueous leaf extract of *S. alata* using wistar rats.

The quantitative phytochemical estimation revealed that aqueous dried leaf 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 (Ahmad et al., 2013). Saponin was 2.83% and can be considered as safe and non-toxic (Asuk et al., 2015) as high levels of saponin >10% have been associated with gastroenteritis, manifested by diarrhoea and dysentery, flavonoids (1.53%), indicating that *S. alata* can help fight against microbes and hepatic toxicity (Georgiev et al., 2014). The results of the proximate composition showed the presence of high crude fibre (53.87%), which is a good indication that the

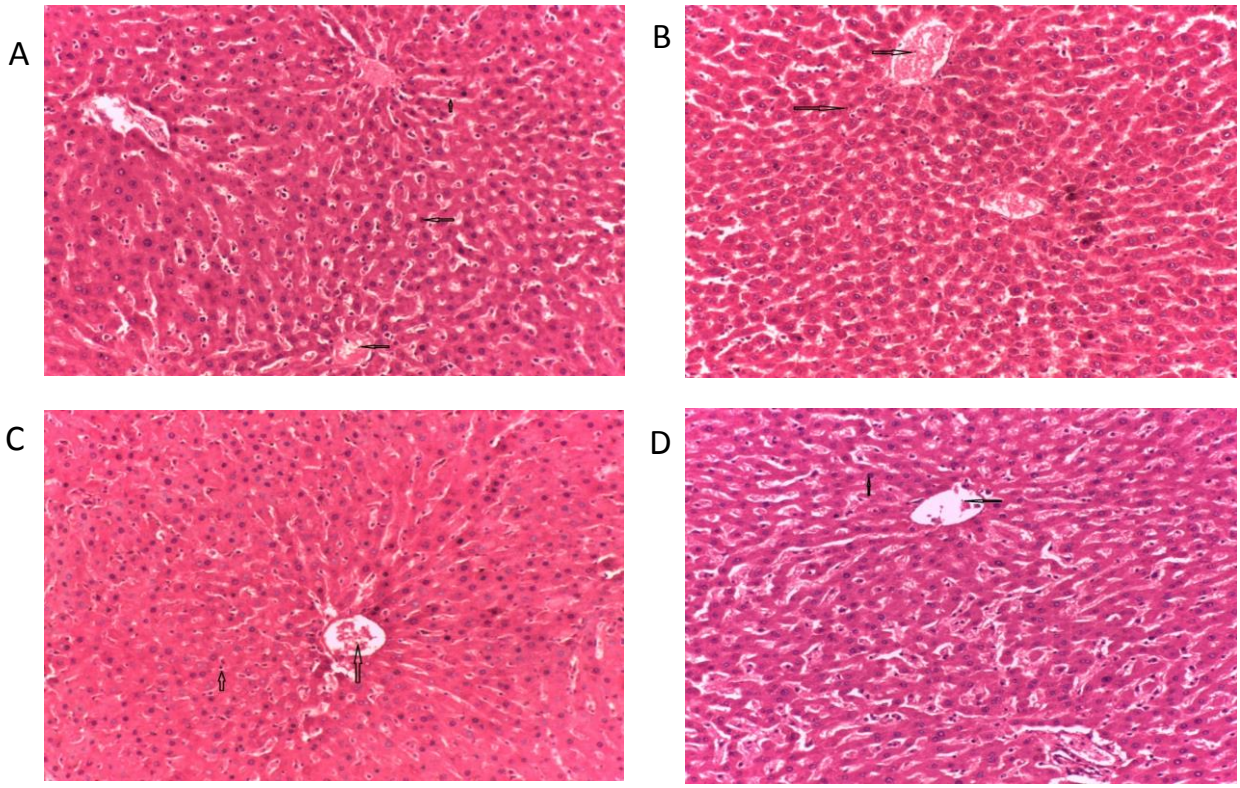

Figure 2. Micrographs of the liver sections obtained from untreated (control) and treated wistar rats with various doses of aqueous dried leaf extract of *Senna alata*. Haematoxylin and eosin staining (H&E), Magnification (40×). (A) control, (B) wistar rats treated with 250 mg/kg leaf extract of *Senna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

plant can prevent diverticulosis and also aid in the absorption of trace elements in the guts (Chiba et al., 2015) and carbohydrate (17.00%), which can serve as energy source while moisture content and ash content fell within the range of acceptable limits (6 to 15%) for most vegetable drugs (Asuk et al., 2015).

The acute toxicity evaluation of the aqueous dried leaf extract of *S. alata* showed no mortality, although scratching of body, calmness, dullness, and weakness of body within 2 h were noticed among rats treated with higher dose of up to 10 g/kg body weight, suggesting LD_{50} of *S. alata* to be above 10.0 g/kg. This result shows that *S. alata* is safe for oral usage at tested doses and can be categorized as non-toxic plant based on report that LD_{50} above 5000 mg/kg body weight is considered as non-toxic (Zbinden and Flury-Roversi, 1981). In the sub-acute toxicity study, there were no significant differences ($P>0.05$) in percentage of weight gain of the rats when compared with the control groups throughout the study, but there was observable general improvement in body weight of all the rats; this weight gain could be attributed to the nutritive constituents present in feed or aqueous leaf extract used (Ashafa et al., 2012). Also, increase or decrease in relative organ weight has been implicated to be a sensitive indicator of organ toxicity (Aly and El-Gendy, 2015). The relative weight of organs (liver, spleen, kidneys, lungs, testes, and heart) were not altered in all the groups treated with *S. alata* when compared with the control rats, thus serving as good indicator that the extract may not be toxic. Similar result was obtained from the findings of Silva et al. (2011) on acute and sub-acute toxicity of *Cassia occidentalis* L. stem and leaf in wistar rats.

The results of all haematological parameters were within the internationally accepted reference range for each tested parameter. Therefore, it could be suggested that the aqueous dried leaf extract of *S. alata* did not produce adverse effect on the bone marrow, which is the chief organ for haematopoietic processes and susceptible targets of toxic compound (Kifayatullah et al., 2015). This implies that *S. alata* may not have negative effects to the immune system since the white blood cell and differential counts are not impaired.

It has been previously reported that some herbal remedies have hepatotoxic (Movahedian et al., 2014) and nephrotoxic effects (Asif, 2012). The maintenance levels within the internationally accepted reference range of creatinine, urea and electrolytes (Na^+, Cl^-, HCO_3^- and K^+) of the wistar rats treated with aqueous dried leaf extract of *S. alata* suggests that the short term treatment of

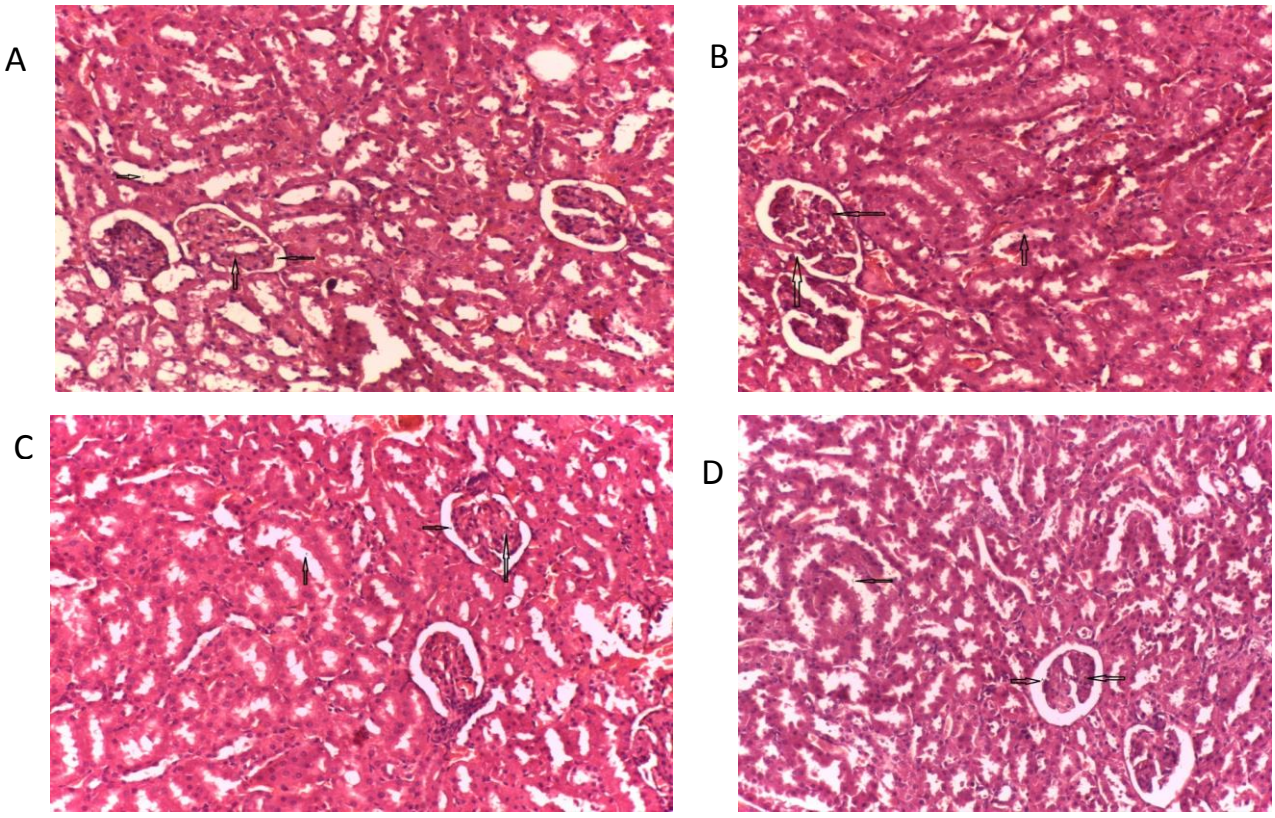

Figure 3. Micrographs of the kidney sections obtained from untreated (control) and treated wistar rats with various doses of aqueous dried leaf extract of *Senna alata*. Haematoxylin and eosin staining (H&E), Magnification (40×). (A), control (B), wistar rats treated with 250 mg/kg leaf extract of *Senna alata*. (C), wistar rats treated with 500 mg/kg leaf extract of *Senna alata*. (D), wistar rats treated with 1000 mg/kg leaf extract of *Senna alata*.

extract has no detrimental effect on the kidney function of the wistar rats. Also, lack of alteration in the liver biomarkers (AST, ALT and ALP) from internationally accepted reference range to the treated wistar rats showed that the administration of the aqueous dried leaf extracts of *S. alata* cannot cause an impairment of liver function of the wistar rats. However, Yagi et al. (1998) reported that ethanol extract and compounds isolated from *S. alata* caused subtle hepatorenal toxicity on rats.

Lipid profile showed slightly higher values at 250 mg/kg dose for total cholesterol, triglycerides, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol when compared with the other doses and the control. Interestingly, the results of all the tested lipid profile parameters were within the internationally accepted reference range for each tested parameters. The histopathological examination of liver and kidney harvested from the control rats and rats treated with various doses of *S. alata* showed that aqueous dried leaf extract of *S. alata* did not damage or produce any pathological changes in the organs.

In conclusion, this study has presented strong evidence that *S. alata* is non-toxic and safe for consumption and for therapeutic uses in folk medicine at the tested doses.

Conflict of interests

The authors have not declared any conflict of interests.

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