European Journal of Medicinal Plants
6(2): 110-123, 2015, Article no.EJMP.2015.048
ISSN: 2231-0894

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Toxicity and Pharmacognostic Standards for Laxative Properties of Nigerian *Cassia sieberiana* and *Senna obtusifolia* Roots

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Authors' contributions

This work was carried out in collaboration between all authors. Author COA managed the literature searches, conducted the physical and biological studies as M. Sc. student of author AAE. Author AAE designed the study, wrote the protocol, supervised the study, wrote the manuscript and processed for publication. Authors RAB and AEO managed the sectioning of tissues and the analysis of histo-pathology slides. Author JAA managed the sectioning by microtomy and analyzed the plant tissue. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/EJMP/2015/14470
Editor(s):
(1) Ahmed Moussa, Institute of Veterinary Sciences University, Algeria.
(2) Marcello Iriti, Department of Agricultural and Environmental Sciences, Milan State University, Italy.
Reviewers:
(1) Anonymous, Nigeria.
(2) Anonymous, India.
(3) Anonymous, Cameroon.
(4) Anonymous, India.
(5) Anonymous, Brazil.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=903&id=13&aid=7642

Original Research Article

Received 30th September 2014
Accepted 3rd December 2014
Published 6th January 2015

ABSTRACT

Aims: Research for sourcing laxative crude drugs among Nigerian *Cassia/Senna* species has continued. The roots of *Cassia sieberiana* and *Senna obtusifolia*, reported as mild laxatives, were subjected to pharmacognostic and toxicity investigations to form part of their monographs.

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Study Design: This is an experimental laboratory report on toxicological and pharmacognostical investigations that will provide some relevant pharmacopoeial standards for these two plants growing in Nigeria.
Place and Duration of Study: Department of Pharmacognosy Obafemi Awolowo University, Ile-Ife Nigeria, between August, 2010 and January, 2013.
Methodology: Roots of *Cassia sieberiana* DC. (Caesalpiniaceae). And *Senna obtusifolia* Irwin and Bernaby (Caesalpiniaceae) were collected from the Eastern (Nsukka), Western (Ile-Ife and Iree) and Northern (Jos) parts of Nigeria during the rainy season. The plant materials were subjected to organoleptic, morphological, phytochemical, physico-chemical and toxicity experiments. The data were analyzed by one-way Analysis of Variance at 95% confidence level. The reference *Senna alexandrina* (Herb Tea), was purchased from a Pharmacy.
Results: The micro-morphological examination of *C. sieberiana* and *S. obtusifolia* roots showed porous vessels, apotracheal parenchyma cells, etc., as valuable diagnostic characters for identification. Free and combined anthraquinones were detected. The toxic oral dose (LD50) for hot infusion of each plant material was found to be > 5000 mg/kg in rats. The histo-pathological examination of *C. sieberiana* at 500 mg/kg and 1000 mg/kg showed a reversible proliferation of the messenchyma cells of the kidney, mild periportal infiltration of the liver and mild to moderate testicular atrophy in rats while for *S. obtusifolia* at 500 mg/kg, no observable histo-pathological changes were observed except at 1000 mg/kg, which showed mild periportal infiltration of the liver as also observed with the infusion of the reference senna.
Conclusion: The results have therefore provided some of the valuable data required for the identification, evaluation, quality assurance and safety on the two plants to qualify them for incorporation into the 2nd editions of the Nigerian Herbal Pharmacopoeia (NHP) and the West African Herbal Pharmacopoeia (WAHP).

Keywords: Cassia sieberiana; Senna obtusifolia; pharmacopoeia; histo-pathology.

1. INTRODUCTION

Cassia sieberiana DC. (Caesalpiniaceae), commonly known as African laburnum, is distributed from Senegal, eastern part of Gambia and Nigeria to the Democratic Republic of Congo, Uganda. In traditional medicine, the plant is used as purgative, antimicrobial, antiviral, antibacterial, anti-inflammatory, antitrypanosomal and antioxidant, diuretic and abortifacient, also to treat schistosomiasis, dysentery and haemorrhoid [1,2]. *Senna obtusifolia* (Linn.) Irwin and Barneby (Caesalpiniaceae), commonly known as African foetid cassia or low senna, was introduced into Africa from America and presently found throughout tropical Africa including Nigeria with the exception of Madagascar. The plant is used as antimicrobial, antifungal, anticancer and antioxidant agents [3]. The leaves are chewed for cough, pneumonia, mixed with other plants for fever, parasitic skin-infections and ulcer [4] while the root is purgative and anthelminthic [5]. *Senna alexandrina* Mill (Senna of commerce), an official pharmacopoeial drug of the same family, widely used as self-help household laxative, is not indigenous to Nigeria though regularly imported from the United Kingdom. Hence, over the years, some other *Cassia* and *Senna* species of Nigerian origin have been screened as possible substitutes for *Senna alexandrina* [6]. Although, the laxative activities of the Nigerian samples of *C. sieberiana* and *S. obtusifolia* roots have been reported by Ajayi et al., [7], no pharmacognostical or toxicological reports of the roots, required for their quality standards and safety limits have been reported. The present study was designed for providing some pharmacopoeial standards and determining the toxicity levels of *C. sieberiana* and *S. obtusifolia* roots in order to qualify them for incorporation into the second editions of the Nigeria Herbal Pharmacopoeia (NHP) and the West African Herbal Pharmacopoeia (WAHP).

2. MATERIALS AND METHODS

2.1 Plant Material

Cassia sieberiana DC. (Caesalpiniaceae), root was collected from Jos in Plateau State, Nsukka in Enugu State and Ile-Ife in Osun State of Nigeria while *Senna obtusifolia* Irwin and Barneby (Caesalpiniaceae) root was also collected from Jos, Nsukka and Iree. The official *Senna alexandrina* Mill (Caesalpinaceae) leaf as the reference standard was purchased from a local Pharmacy shop in Ile-Ife as “Herb Tea”,

imported into Nigeria from Darkin's Brothers in London. The identities of the two plants were confirmed, after an on-the-field identification, followed by authentication by direct comparison of their herbarium specimens with the samples of previously collected and preserved *C. sieberiana* and *S. obtusifolia*, respectively, in the Forest Research Institute of Nigeria (FRIN), Ibadan with the FHI numbers 109561 and 109562, respectively. The roots were cut into small pieces and oven-dried for 48 h at 50°C, powdered, stored in sealed amber bottles and kept in a dry cupboard until ready for use.

2.2 Organoleptic Tests

The shape, size, colour, surface character, odour and taste of the roots were studied according to the method of Okpon [8]

2.3 Microscopy

The microscopical studies of the transverse section, tangential longitudinal section and fibres of the root were prepared and stained in accordance with the procedure of Olatunji [9] and viewed under the microscope at 15,000 µm magnification.

2.4 Phytochemical Tests

To 5 g of the powdered root, 100 mL boiling distilled water was added and left for 15 minutes and filtered [10]. 50 mL of the filterate (the infusion) was shaken with 10 mL of diethyl ether in a separating funnel. The ethereal layer was separated and tested with 5 mL of dilute ammonia solution. A pink to rose pink colouration indicated a positive reaction for free anthraquinones [11]. The infusion was boiled with HCl and further extracted with 5 x 10 mL of diethyl ether in a separating funnel. The ethereal layer was separated and tested with 5 mL of dilute ammonia solution. A pink colour indicated combined anthraquinones.

2.5 Physicochemical Constants

The percentage total, acid-insoluble and water-soluble ash values as well as water- and alcohol-soluble extractives, were determined following the African Pharmacopoeial methods of 1986 [12]. The alcohol- and water-soluble extractives, the plants's histochemistry and moisture contents were each determined as the average of twelve replicate samples following the African Pharmacopoeia [12] methods.

2.6 Toxicological Studies

2.6.1 Animals

White wistar male rats weighing between 95 and 215 g were purchased from the animal house of the Faculty of Basic Medical Sciences, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria. The animals were housed in wire-netted cages and kept in the animal house of the Department of Pharmacology, Obafemi Awolowo University, Ile-Ife, Nigeria. They were fed with rat cubes purchased from Capsfeed Limited and the rats were served with water regularly. All animals were cared for in accordance with the Guide for the Care and Use of Laboratory Animals, published by the US National Institute of Health [13].

2.6.2 Preparation of infusion

A standard concentration equivalent to 100 mg/mL of powdered drug was prepared by placing 5 g of the powdered drug (*C. sieberiana* root, *S. obtusifolia* root and *S. alexandrina* (Herb Tea) in 50 mL boiling distilled water in a conical flask. This was covered and kept aside for 15 mins, filtered using sieve nos. 2000 and 710. An aliquot was taken and orally administered to the rat at a pre-determined dose [2].

2.6.3 Acute toxicity

This was carried out using the method of Lorke [14]. In the first phase, nine rats were randomly divided into three groups of three rats each and each group received the infusion of *C. sieberiana* root or *S. obtusifolia* root or *S. alexandrina* leaf at 10, 100 and 1000 mg/kg body weight orally (*via* a feeding cannula), respectively. The rats were then observed for signs of adverse effects and deaths for 48 h and 14 days, respectively [14]. In the second phase, four rats were divided into 4 groups of 1 rat each and were each similarly treated with the infusion of *C. sieberiana* root or *S. obtusifolia* root or *S. alexandrina* leaf at doses of 1000, 1600, 2900 and 5000 mg/kg orally [14]. The rats were weighed daily, and then observed for signs of toxicity such as paw-licking, salivation, stretching, rubbing of nose on the floor, walls of the cages and mortality. The numbers of deaths in each group within 48 h and after 14 days were recorded and the final LD_{50} values calculated as the geometric mean of the highest non-lethal dose and the lowest lethal dose.

LD_{50} = [A× B] ^{½} A= the highest non lethal dose, B= the lowest lethal dose

2.6.4 Sub-chronic toxicity

Forty (40) male Wister albino rats were randomly distributed into ten groups of four rats. Groups I, II and III received *C. sieberiana* root infusion at doses of 250, 500 and 1000 mg/kg orally, respectively; Groups IV, V, and VI received similar doses of *S. obtusifolia* root while Groups VII, VIII and IX received similar doses of Herb Tea (*S. alexandrina* leaf as reference drug). Then, Group X received 0.5 mL distilled water as negative control. These animals received their respective doses once a week for four weeks and had free access to food and water and were examined daily for signs of toxicity. At the end of four weeks, the animals were sacrificed under chloroform anaesthesia, autopsied and examined macroscopically for any organ pathological changes. The liver, kidney, testis and brain were removed, grossly observed for any pathological changes while 5 µ-thick sections of the organs were fixed with 10% formalin, embedded in paraffin and stained with haematoxylin and eosin (H and E) for histological analysis [15]. The slides were later viewed under the microscope at magnification of 100, followed by photomicrography.

3. RESULTS

The macroscopical features of *C. sieberiana* root showed brown to dark brown colour, branched, wide, the powdered root showed faint yellow in colour, odourless with slightly bitter taste. The microscopical features showed outer bark with several layers of dead thick-walled cells whose shapes were rectangularly or cylindrically elongated. Inner bark was made up of living thick-walled parenchymatous cells of various shapes (Plate 1a). Presence of tannins in the inner bark of the root; brachysclereid, formed a round circle within the inner bark. The sclereids were majorly in the inner bark; starch granules also present; vessels were diffuse, porous, pore circular, oval, arch in shape; clustered of 2–7, and predominantly multiple of 2-11 while solitary vessels were few, with the presence of tyloses; axial parenchyma cells were apotracheal with the presence of uniseriate, biseriate, multiseriate, heterogeneous, upright and procumbent medullary rays (Plate 1b). Vessel elements present with boardered pits, some having tails at both ends while others have no tail; fibres were non-storeyed, non-septate, large lumen with narrow wall (Plates 1c& d).

Similarly, the macroscopical features of *S. obtusifolia* root showed cylindrical shape, branched, varying in size with respect to age but mostly 9–25-30 cm long and 0.8–1.7–2.3 cm wide, brown to dark brown colour, occasionally smooth, closely annulated, bearing rootless and hairs. The microscopy features showed a thin epidermis, cortex, white to slight yellow in colour, outer bark is made up of 4-6 layers of dead rectangular, oval, circular or polygonal cells in shape. The inner bark is made up of several layers of living thick-walled parenchymatous cells (Plate 2a). Tannins present, sclereids absent with the crystal druses in the inner bark. Vessels were diffuse, porous system, pore clustered of 2 -13, multiple of 2-8 and solitary vessels present. Vessels were almost of equal number unlike *C. sieberiana*. Pore-shaped, circular, oval, arch and short rectangular; tyloses present in few pores, axial parenchyma cells also apotracheal and diffuse with the presence of uniseriate, biseriate, homogeneous and predominant medullary rays (Plate 2b). Presence of starch granules and vessel elements with boardered pits, some with tails at both ends, some at one end while others have no tail. Non- storeyed and non-septate fibres with large lumens and narrow walls (Plates 2c & d).

The general chemical tests for anthraquinones in the three species (*C. sieberiana*, *S. obtusifolia* and *S. alexandrina*) revealed the presence of both free and combined anthraquinones.

The results of the acute toxicity revealed no death with doses up to 5000 mg/kg of *S. alexandrina* leaf (reference), *C. sieberiana* and *S. obtusifolia* root infusions after 48 hours and 14 days of observation which showed that the LD_{50} was > 5000 mg/kg and they were acutely not toxic and showed no significant difference in the weight gained by the animals in all doses (Tables 3 and 4). However, at doses above 1000 mg/kg, the initial reactions from the rats showed excitement, reduced appetite, restlessness and subsequently reduced activity with *S. alexandrina* leaf (reference), *C. sieberiana* and *S. obtusifolia* root infusions. In the sub-chronic toxicity experiments, the histopathological examination of the organs of animals dosed with 0.5 mL distilled water (negative control) showed essentially normal features with no damage to any brain cell (Plate 3a) while the tubules in most part of the kidney were essentially normal

(Plate 4a). The liver showed a mild to moderate congestion of the central veins, while the parenchyma was essentially normal (Plate 5a). The testis showed normal cells of the spermatogenetic series whereas there was no inflammation of the interstitial fibrosis (Plate 6a). The histological examination of the organs of animals dosed with the infusion of *S. alexandrina* leaf (positive control) at 500 and 1000 mg/kg, showed an essentially normal brain with no damage to any brain cell (Plates 3b and 7b); the kidney tubules in most part of the kidney were essentially normal (Plate 4b and 8b). The liver of the animal dosed with the infusion of *S. alexandrina* leaf (positive control) at 1000 mg/kg showed a mild to moderate congestion of the central veins while the parenchyma was essentially normal as shown in Plate 9b.

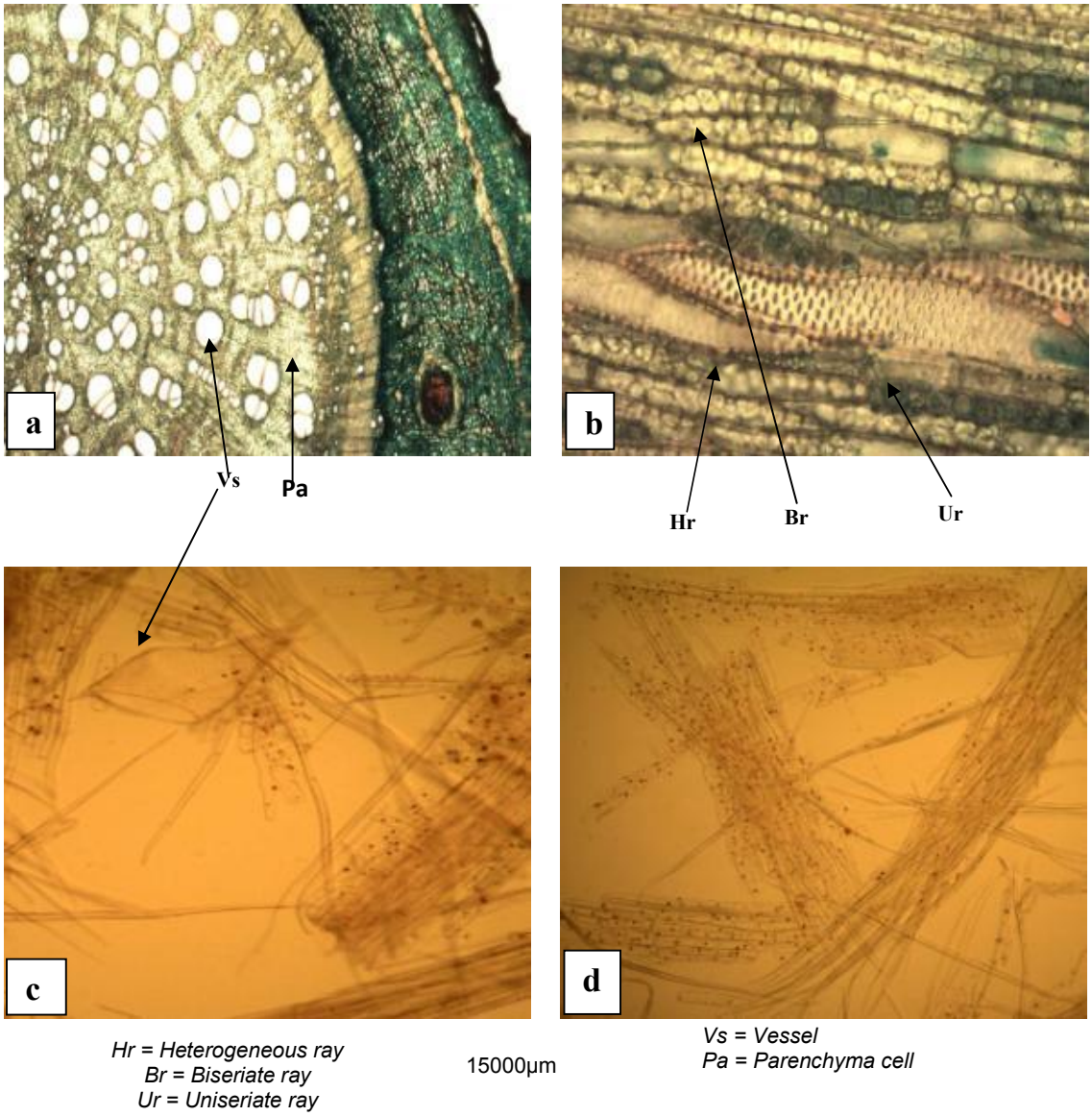

Plate 1. Photomicrographs of (a) transverse section, (b) tangential longitudinal section and (c and d) fibres of the root of *C. sieberiana*

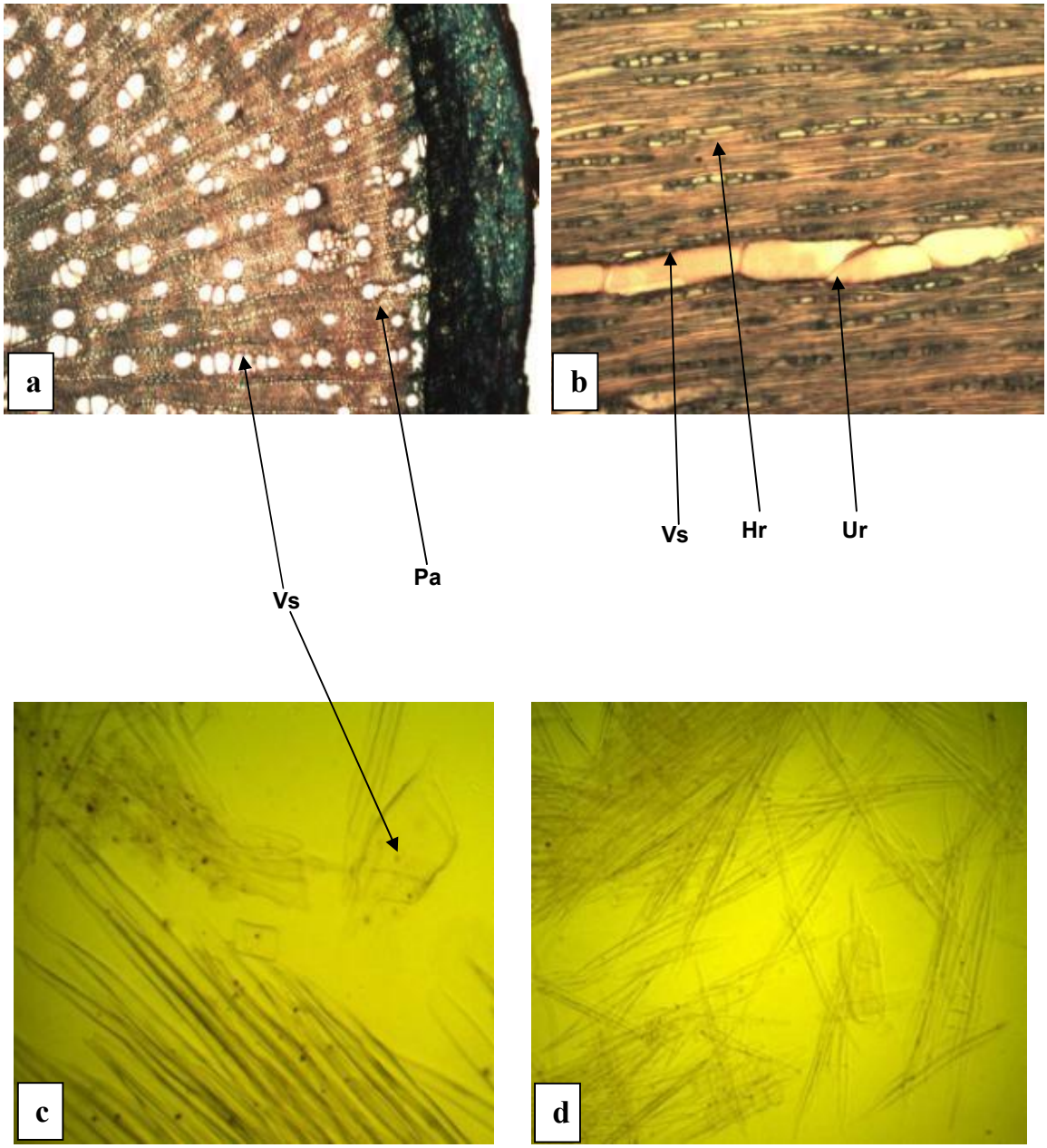

Plate 2. Photomicrographs of (a) transverse section, (b) tangential longitudinal section and (c and d) fibres of the root of *S. obtusifolia*

The testis showed normal cells of the spermatogenetic series and there was no inflammation of the interstitial fibrosis (Plate 10b). The histopathological examination of the organs of animals dosed at the sub-chronic levels with *C. sieberiana* root infusion at 500mg/kg showed an essentially normal brain and normal kidney (Plates 3c and 4c), while the liver showed a mild to moderate congestion of the central veins though the parenchyma was essentially normal (Plate 5c). However, the testis showed mild to moderate thickness of the basement membrane,

loss of cells of spermatogenetic series and interstitial fibrosis with mild hypertrophies of the leygid cells and mild to moderate testicular atrophy (Plate 6c). *C. sieberiana* root infusion at 1000 mg/kg on the kidney also showed a proliferation of the messenchyma cells and narrowing of the Bowman space in areas but the tubules and interstitial space were initially normal as in Plate 8c. The liver also showed a mild to moderate congestion of the central veins with mild dilation of the sinosis and mild periportal infiltration by inflammatory cells (Plate 9c). Also, at 1000 mg/kg the testis showed mild to moderate thickness of the basement membrane, loss of cells of spermatogenetic series and interstitial fibrosis with mild hypertrophies of the leygid cells and mild to moderate testicular atrophy (Plate 10c). The histopathological result of the organs of animals dosed at the sub-chronic levels with *S. obtusifolia* root infusion at 500 mg/kg showed a normal brain (Plate 3d), kidney (Plate 4d), liver (Plate 5d) and testis (Plate 6d) while at 1000 mg/kg there was a mild to moderate congestion of the central veins of the liver, mild dilation of the sinosis and mild periportal infiltration (Plate 9d). Meanwhile, there were normal cells of the spermatogenetic series and no inflammation of the interstitial fibrosis of the testis was found (Plate 10d).

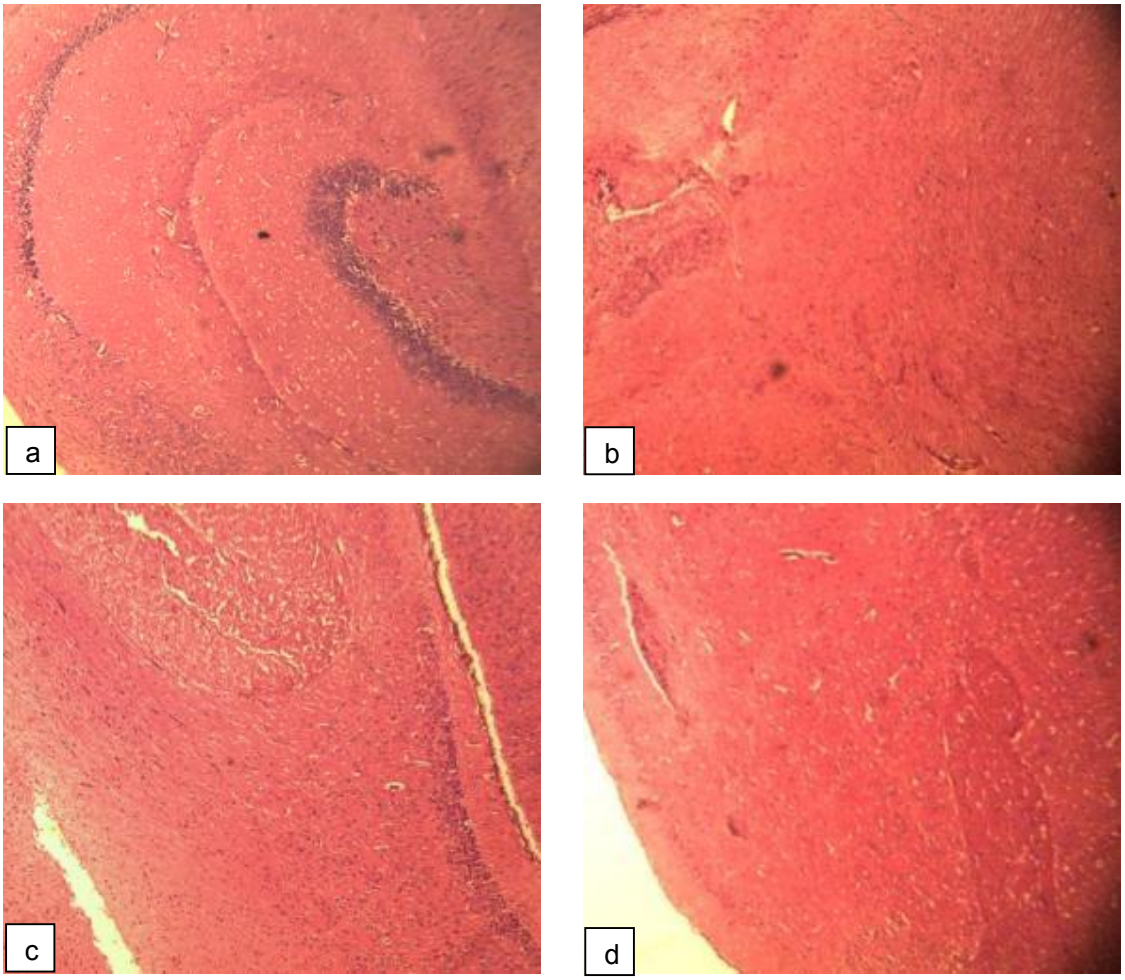

Plate 3. Photomicrograph of a section of Brain of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *Senna alexandrina* (b), *Cassia sieberiana* (c) and *Senna obtusifolia* (d) at 500 mg/kg showing essentially normal cell (H & E ×100)

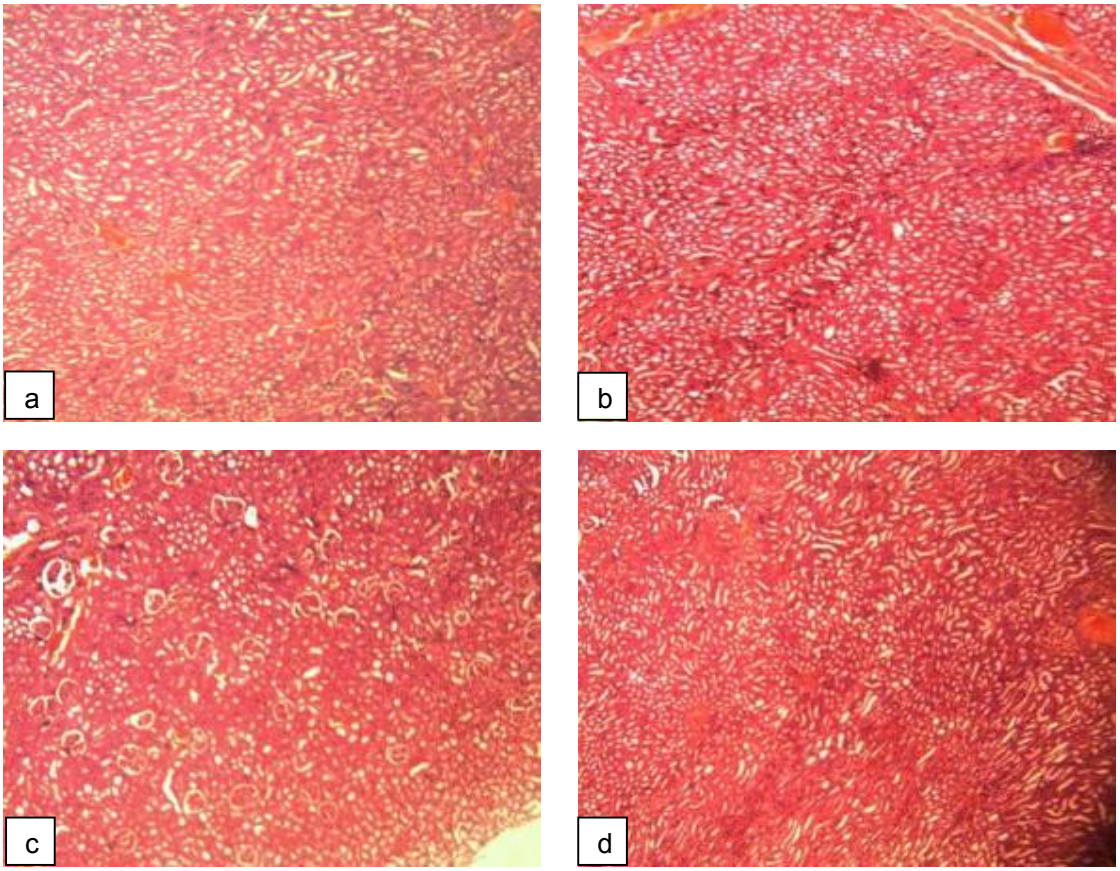

Plate 4. Photomicrograph of a section of Kidney of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 500 mg/kg showing normal cell (H & E ×100)

Table 1. Percentage ash values of *C. sieberiana* and *S. obtusifolia* roots

Location	*C. sieberiana*			*S. obtusifolia*		
	Total ash	Acid-insoluble ash	Water-soluble ash	Total ash	Acid-insoluble ash	Water-soluble ash
East	2.0±0.01*	0.4±0.01*	0.5±0.01*[a]	3.2±0.02*	0.8±0.02	1.6±0.02
West	2.4±0.02*	0.5±0.01*	0.6±0.01*[a]	4.3±0.1*	0.9±0.01	1.7±0.04
North	2.1±0.07*	0.3±0.003*	0.5±0.22[a]	3.9±0.04*	0.4±0.01*	1.7±0.03
Average	2.2±0.1	0.4±0.1	0.5±0.03	3.8±0.3	0.7±0.2	1.7±0.03

*All data were expressed as Mean ± SEM, n=12 *P < 0.001, [a] P < 0.01*

Table 2. Percentage extractive values and moisture contents of *C. sieberiana* and *S. obtusifolia* root

Location	C. sieberiana			*S. obtusifolia*		
	Alcohol-soluble	Water-soluble	Moisture content	Alcohol-soluble	Water-soluble	Moisture content
East	6.8±0.1*	6.2±0.9*	10.9±0.02*	8.1±0.1	6.9±0.1*	9.1±0.03
West	7.8±0.1*	7.3±0.1[b]	8.1±0.1*	7.1±0.7*	7.6±0.1*	8.4±0.1*
North	10.1±0.04*	7.0±0.1[b]	9.5±0.1*	8.1±0.1	8.2±0.1*	9.0±0.1
Average	8.2±1.0	6.8±0.3	9.5±0.8	7.8±0.3	7.6±0.4	8.8±0.2

*All data were expressed as Mean ± SEM, n=12, *P < 0.001, [b] P < 0.05*

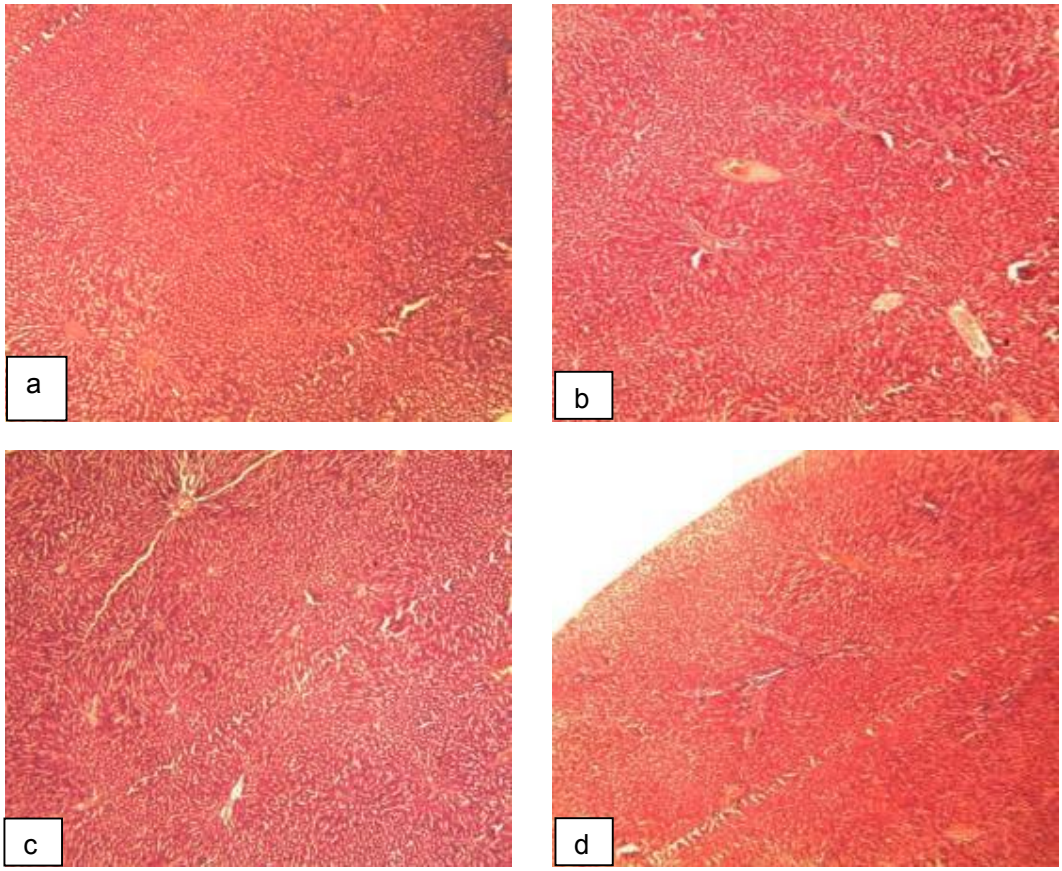

Plate 5. Photomicrograph of a section of Liver of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 500 mg/kg showing a mild to moderate congestion of the central veins (H & E ×100)

Table 3. Acute response on body weights in rats treated with infusions of *S. alexandrina* leaf, *C. sieberiana* root and *S. obtusifolia* root

Dose/Plant material	10 mg/kg		100 mg/kg		1000 mg/kg	
	Final body weight	Mean weight gain	Final body weight	Mean weight gain	Final body weight	Mean weight Gain
S. alexandrina	157.0±16.5	9.0±2.7	154.7±2.4	7.0±1.0	146.0±6.9	6.3±2.0
C. sieberiana	163.0±5.3	11.3±0.9	159.0±5.5	8.0±1.5	158.0±0.6	8.0±0.6
S. obtusifolia	162.3±3.4	10.7±1.2	160.7±7.8	9.0±2.3	163.0±7.7	8.0±3.2

*All data were expressed as Mean ± SEM, n=3, *P < 0.05*

Table 4. Acute response on body weight and % weight gain in rats treated with infusions of *S. alexandrina* leaf, *C. sieberiana* root and *S. obtusifolia* root

Dose/Plant material	1600 mg/kg		2900 mg/kg		5000 mg/kg	
	Final body weight	Mean weight gain	Final body weight	Mean weight gain	Final body weight	Mean weight gain
S. alexandrina	160	7	150	6	146	5
C. sieberiana	145	8	170	5	158	5
S. obtusifolia	170	7	175	7	163	6

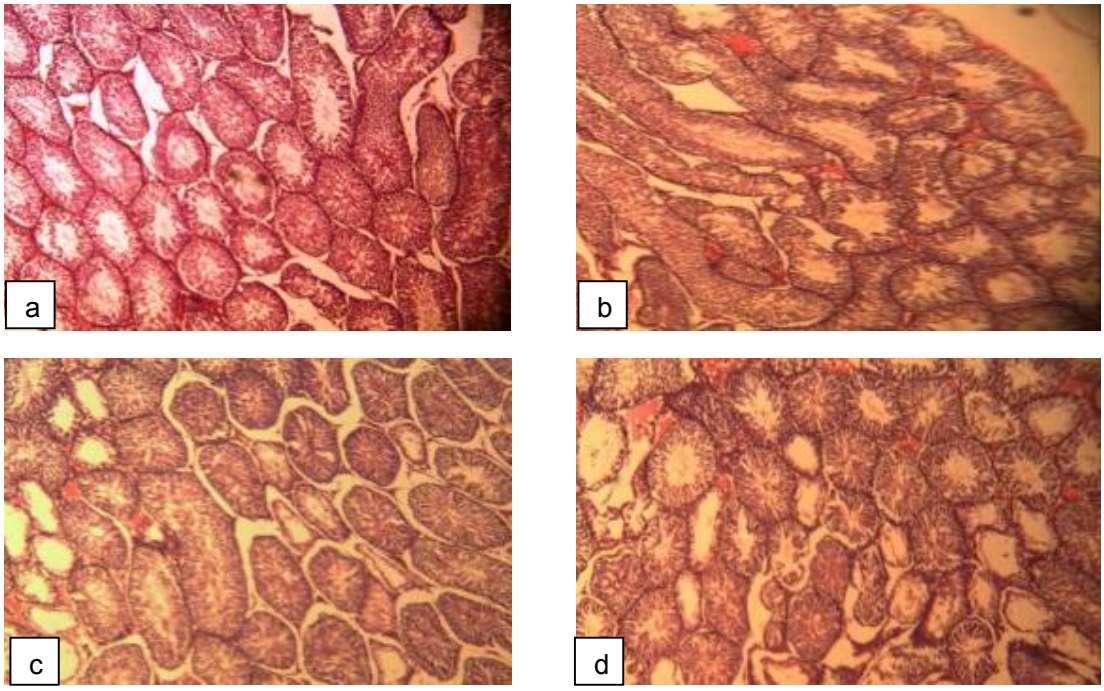

Plate 6. Photomicrograph of a section of Testis of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 500 mg/kg showing loss of cells of spermatogenetic series and interstitial fibrosis with mild hypertrophies of the leygid cells and mild to moderate testicular atrophy in 6c (H & E ×100)

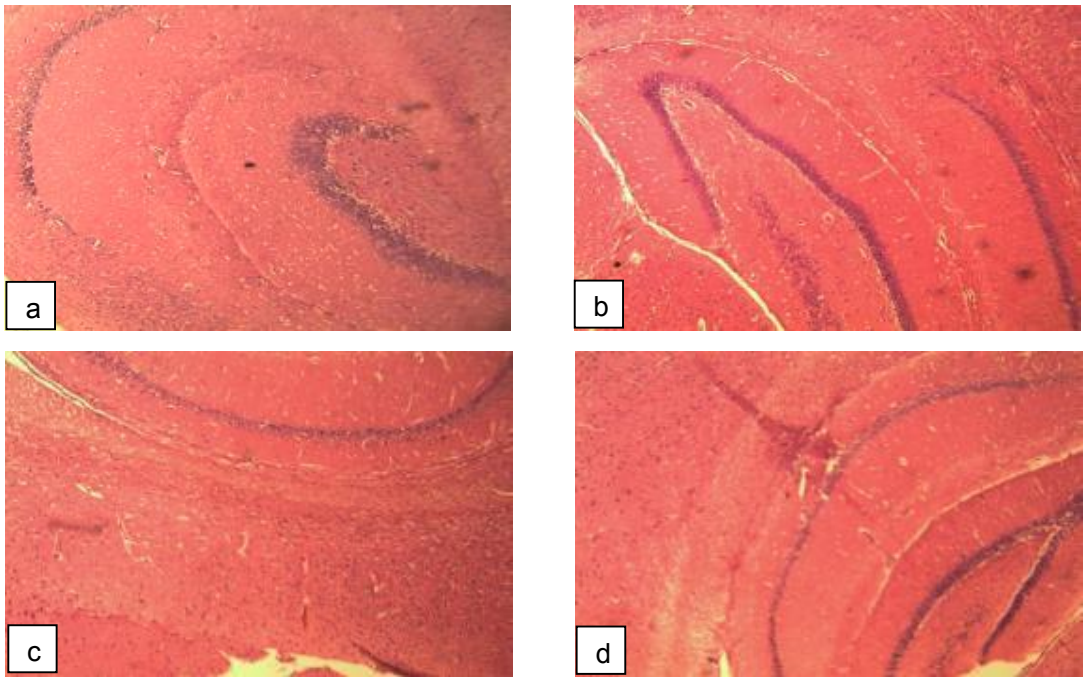

Plate 7. Photomicrograph of a section of Brain of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 1000 mg/kg dose showing essentially normal cell (H & E ×100)

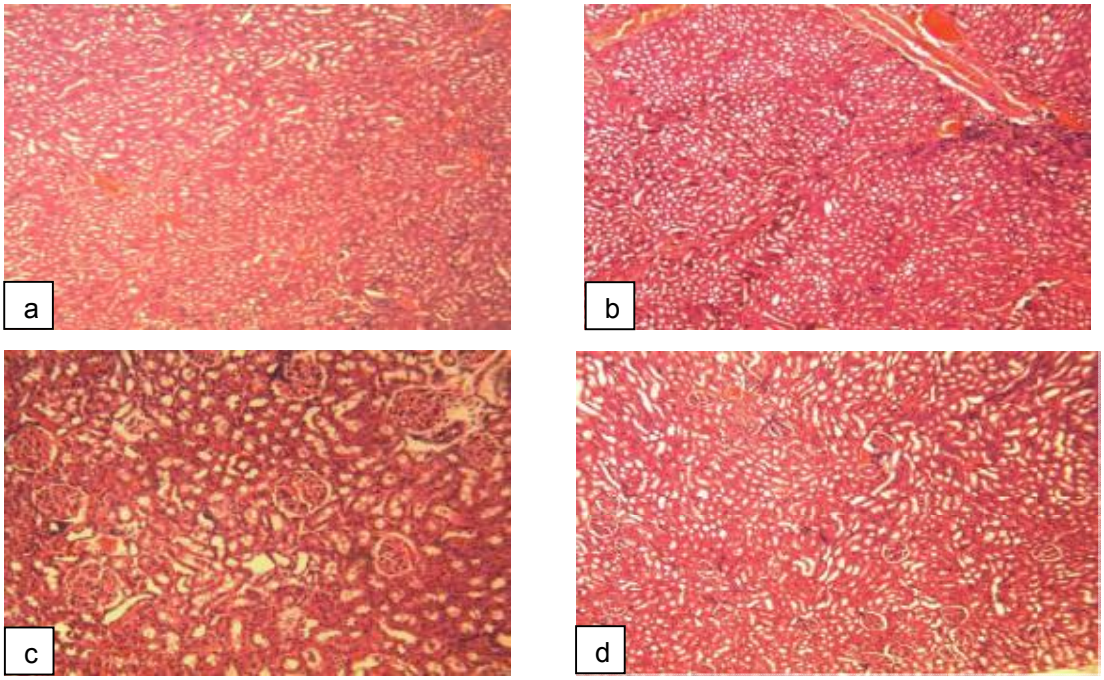

Plate 8. Photomicrograph of a section of Kidney of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 1000 mg/kg dose showing a proliferation of the messenchyma cells and narrowing of the Bowman space in areas in 8c (H & E ×100)

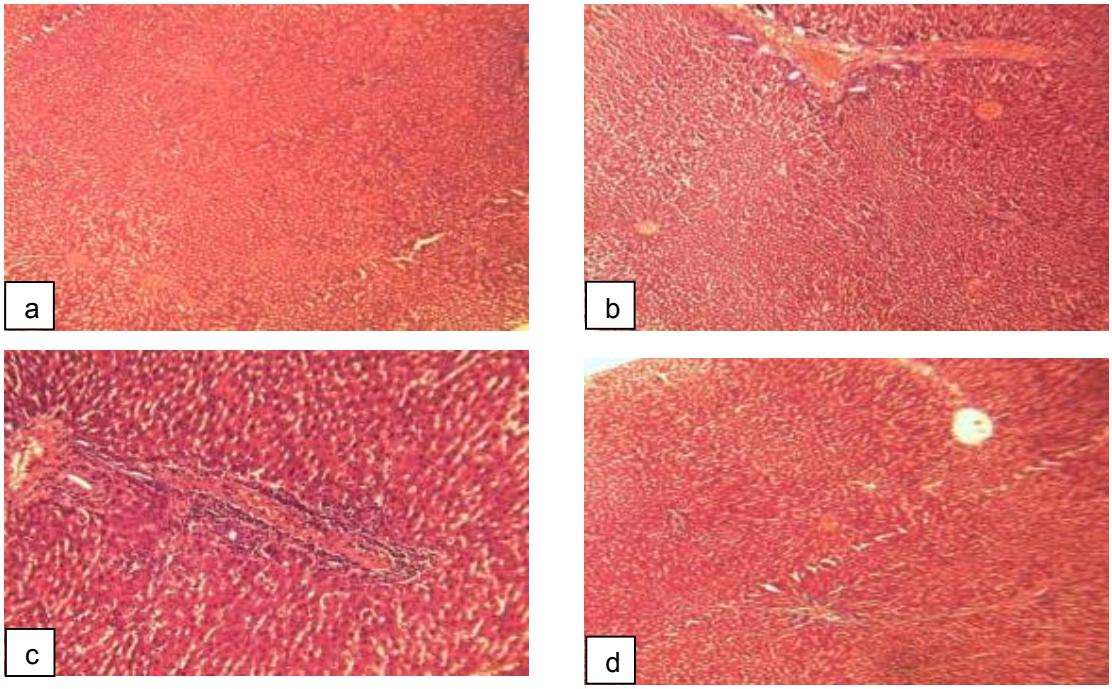

Plate 9. Photomicrograph of a section of liver of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 1000 mg/kg dose showing mild to moderate congestion of the central veins, mild dilation of the sinosis and mild periportal infiltration (H & E ×100)

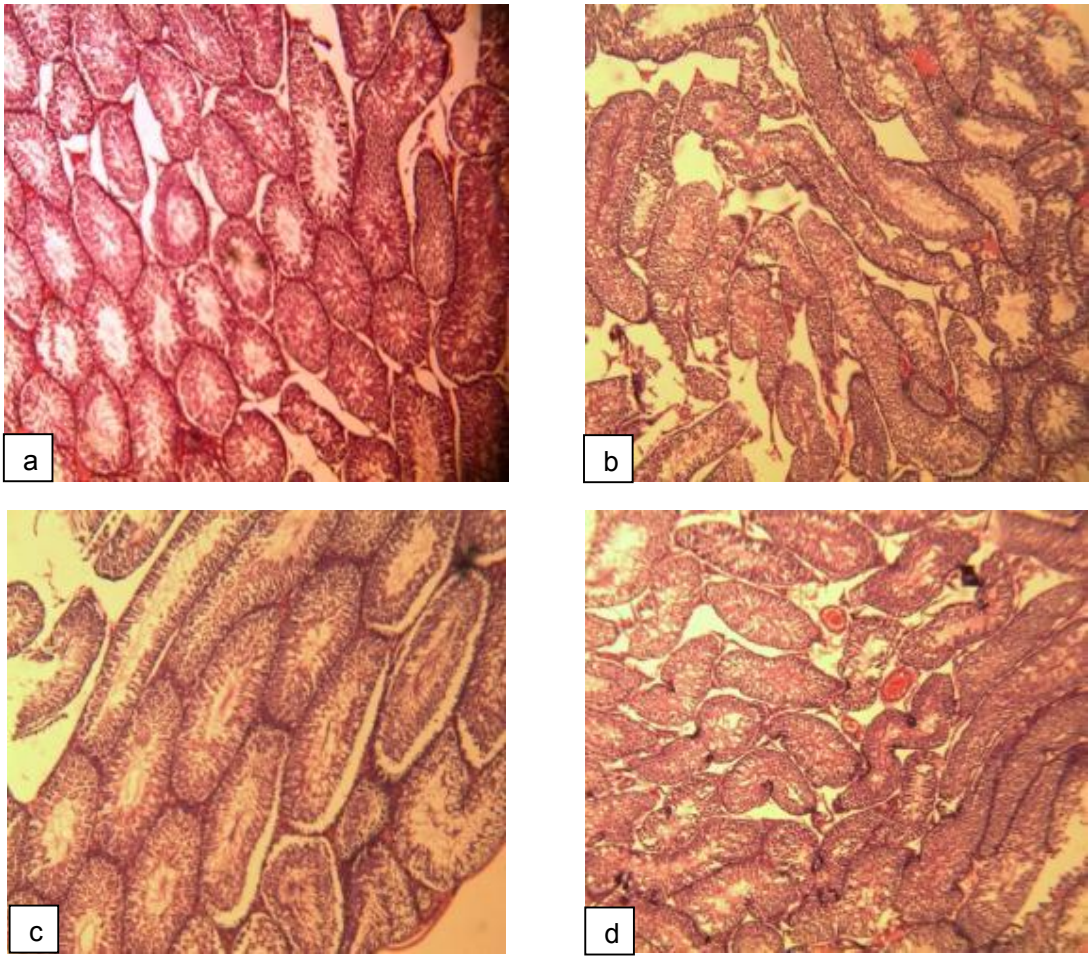

Plate 10. Photomicrograph of a section of Testis of the control rat (a) or rat treated with repeated administration of the aqueous infusion of *S. alexandrina* (b), *C. sieberiana* (c) and *S. obtusifolia* (d) at 1000 mg/kg showing mild to moderate thickness of the basement membrane, loss of cells of spermatogenetic series, mild hypertrophies of the leygid cells and mild to moderate testicular atrophy in 10c (H & E ×100)

4. DISCUSSION

The types and thickening patterns of the xylem vessels, the presence or absence of homogeneous medullary rays, and difference in parenchyma cells are diagnostic features of taxonomic and quality control importance. The range of values obtained for the respective average total ash values for *Cassia sieberiana* root {2.04±0.01–2.35±0.02} and *S. obtusifolia* root {3.15±0.19–4.39±0.05} vary slightly in relation to the geographical locations attributed to possible varying mineral contents in the soil. The percentage acid-insoluble ash value range for *C. sieberiana* root was between 0.31±0.003 and 0.51±0.01 while that of *S. obtusifolia* root was found to be 0.39±0.01 and 0.87±0.01 as shown in Table 1. These values indicate low amounts of silica especially sand as well as siliceous earth present in the two plant species investigated [12]. *S. obtusifolia* root gave percentage water-soluble ash range of between 1.64±0.02 and 1.74±0.03 while *C. sieberiana* root gave 0.41±0.01 and 0.60±0.01. The percentage moisture content range for *C. sieberiana* root was found to fall between 8.12±0.06 and 10.87±0.01 while for that of *S. obtusifolia* root; the range fell between 8.44±0.05 and 9.08±0.03 (Table 2). The results of the soluble-extractive values showed that the chemical constituents of the plant materials were extracted slightly more efficiently into 70% ethanol than 0.5% chloroform-water as shown in

Table 2. Medicinal plants containing anthraquinone glycosides are known to possess laxative activities [16]. Previous *in vivo* studies have shown the resistance of mice and female rats to the laxative efficacy of anthraquinone C-glycosides [17], hence we have used only male wistar rats in our earlier laxative report [7] and for uniformity with the present toxicological investigations, male rats were also used. Acute toxicity experiment indicated a low toxicity (LD_{50} > 5,000 mg/kg) for *C. sieberiana*, *S. obtusifolia* and *S. alexandrina* leaf in rats. Using this result and the fact that 500 mg/kg was recommended by our earlier work as the dose that will produce a significant laxative activity by any *Cassia/Senna* species [7], the following doses: 250, 500 and 1000 mg/kg were used in the present study. The degeneration of tissues shown in the kidney of animals dosed with *C. sieberiana* root infusion at 500 and 1000 mg/kg could lead to glomerulosclerosis. There are also diagnostic atrophies of the testis, mild dilation of the sinosis, periportal infiltration of cells of the liver and observed reduction in spermatogenesis. This correlates with the result of Donkor et al. [18] on the root bark of the same plant collected in Ghana which showed histopathological effect of centrilobular necrosis of the liver at the dose of 750 mg/kg. Furthermore, in the present report, the liver of the animal dosed with the infusion of *S. alexandrina* leaf (positive control) at 1000 mg/kg showed a mild to moderate congestion of the central veins while the parenchyma was essentially normal. The testis showed the normal cells of the spermatogenetic series and there was no inflammation of the interstitial fibrosis. Our result correlates with that of Adefemi et al. [19] which showed a degenerative effect at 1.33 g/kg dose level.

5. CONCLUSION

C. sieberiana root was relatively non-toxic at lower doses whileits toxicity at high doses on the kidney, liver and testis were reversible following withdrawal of the drug. However, for *S. obtusifolia* and *S. alexandrina* [reference drug], there were no toxic effects at both 250 and 500 mg/kg whereas at 1000 mg/kg, the liver showed toxic effect that was reversible on withdrawal. The roots of the two species could therefore be developed as mild laxative drugs for the Nigerian market as substitutes for the official senna and can be incorporated into the second editions of the Nigeria Herbal Pharmacopoeia (NHP) and the West African Herbal Pharmacopoeia (WAHP).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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