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Evaluation of the adverse effects of *Dracaena steudneri* Engl. stem bark aqueous extract in Wistar rats

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Safety of medicinal plants/products is one of the major areas that require more attention because of the high rate at which consumers use medicinal plants/products due to their availability and accessibility. *Dracaena steudneri* Engl. is among the plants being used and recommended for the treatment of several diseases for decades among the traditional health practitioners. Despite its frequent use, there is little literature on its safety. This study investigated the acute and sub-acute effects of *D. steudneri* Engl. stem bark with a view to establishing its safe dose for drug development. The stem bark of *D. steudneri* Engl (Dracaenaceae) was collected, authenticated, dried, pulverized mechanically and extracted using decoction method. The extract was thereafter concentrated *in vacuo* at 50°C using rotary evaporator and lyophilised. The acute test was studied in Wistar rats using Lorke's method at 10 to 5000 mg/kg to determine the lethal dose (LD_{50}) and other adverse effects including weight loss, body scratching etc. In sub-acute test, 24 Wistar rats of both sexes were separately caged and orally administered with extract at 25 to 100 mg/kg. The administration was repeated for 28 days before the animals were humanely sacrificed. Blood of each animal was collected for hematological and biochemical examination, while the essential organs were harvested for histopathologic. The results showed that LD_{50} was greater than 5000 mg/kg. The extract did not exhibit any significant difference ($p>0.05$) on hematological parameters when compared with the negative control. There was no degenerative effect in the histology and pathology of all the organs examined but elevation in serum ALT and creatinine levels was observed. Although the aqueous extract of *D. stuedneri* stem bark did not show any significant hematological and histopathological effect on the organs tested, there was potential for renal and hepatic toxicity after repeated administration. Therefore caution must be taken with close monitoring during prolonged administration.

Key words: Acute, safety, *Dracaena steudneri*, sub-acute, toxicity.

INTRODUCTION

The use of medicinal plants is the most ancient form of treatment (WHO, 2002), and till date it has been the source of novel drugs in drug development (Patil and Gaikwad, 2010). The World Health Organization (WHO,

2002) report indicated that a high number of the world's population depends on herbal medicines for treatment of various diseases being the most accessible, available and widely distributed. However, despite the wide use of these medicinal plants for therapeutic purposes, the users take less concern about their safety (WHO, 2003).

Amongst the commonly used medicinal plants for therapeutic purposes in Uganda is *Dracaena steudneri* Engl, in the family Dracaenaceae. The plant which is commonly known as bush-night fighter and locally known as Sangalyanjovu among the Busoga in Uganda, is a tree 25 m high with a single stem of up to 45 cm in diameter comprising a branched crown clustered leaves. It is abundant in forest and savannah regions including Angola, Burundi, Ethiopia, Kenya, Malawi, Mozambique, Rwanda, Sudan, Tanzania, Uganda, Zambia, and Zimbabwe (Burrows and Willis, 2005).

The whole plant is generally used in the communities for cough while the stem bark extract is used traditionally, for induction of labor and achievement of relatively painless delivery (Tugume et al., 2016). In addition to its use of stem bark for child birth, its leaf is used for treating hernia, splenomegaly, asthma and related chest problems in children, fibroids and infertility in women (Moshi et al., 2007). Also, the decoction of the plant is used for malaria and to ease delivery. The plant has been reported to possess antifungal activity as it was able to inhibit the growth of *Candida albicans*, *Aspergillus* species and *Cryptococcus neoformans* at a low concentration below 12 µg/mL *in vitro* (Kisangau et al., 2014). While i*n vivo* anti-candida activity of the aqueous extract of the plant was reported to have shown a dose dependent activity from 100 to 400 mg/kg in rats (Kisangau et al., 2014). The stem bark of *D. steudneri* is widely used in Busoga, Eastern region of Uganda for painless childbirth.

However, despite its wide use in Uganda for child birth, there was no scientific evidence on its safety. Therefore, this study evaluated the acute toxicity and repeated administration of the aqueous extract of *D. stuedneri* stem bark in Wistar rats for its safety assurance among the users.

MATERIALS AND METHODS

Collection of plant

Fresh *D. steudneri* Engl. stem bark was collected from Bususwa Village in Jinja district (0.5990°N, 33.1239°E), Uganda. The identification and authentication of the plant was done at the herbarium of Makerere University, Kampala, by a taxonomist, Mr Protase before the voucher specimen was deposited and given a voucher number: 001/MGT.

Preparation of aqueous extract of *D. steudneri* Engl. stem bark

Stem bark of *D. steudneri* was washed with water to remove dirt, chopped into small pieces for quick and easy drying and were oven dried at 40°C and pulverized mechanically to coarse powder. The powdered material was extracted by decoction method in which 250 g of powdered material was weighed into a round bottomed flask containing 1 L of distilled water and boiled at 80°C for 45 min (Sofowora and Adesanya 1983). The decocted extract was filtered using Muslin cloth and later with Whatman filter paper No. 1, concentrated *in vacuo* using a rotary evaporator (IKA® RV10) at 55°C to dryness and stored at 4°C until required for further analyses.

High performance liquid chromatography (HPLC) fingerprint of *D. steudneri* extract

The HPLC fingerprint of the aqueous extract *D. steudneri* stem bark extract was performed in order to establish its reproducibility using a *UFLC* Shimadzu Prominence Model HPLC system (Tokyo, Japan) at the Analytical and Pharmaceutical Laboratory, Mbarara University of Science and Technology, Uganda. The equipment comprises a LC-20AD pump, a Phenomenex Luna C_{18} column (250 × 4.6 mm; 5 µm), temperature-controlled sample trays, an online degasser DGU-20A5R and an ultraviolet (UV) detector.

A known concentration of 1 mg/mL aqueous extract of *D. steudneri* stem bark was prepared by dissolving the 10 mg of the extract in 10 mL deionized water. Solvents and deionized water were filtered through a 0.45 µm prior to the analysis. A reversed-phase HPLC assay was carried out using a binary isocratic elution with a flow rate of 1.0 mL/min at a column temperature of 30°C, a mobile phase of methanol/acetonitrile/0.01% trifluoroacetic acid (6:1:3). The injection volume was 10 µL at a detection wavelength of 370 nm. All solvents used were of HPLC grade.

Experimental animals

White Wistar rats of both sexes weighing 120 to 150 g were purchased and housed in the Animal Facility of Mbarara University of Science and Technology (MUST). The animals were kept under a 12-h light/dark cycle with free access to water and were fed with animal feed pellets purchased from NUVITA. They were acclimatized for two weeks prior to the assay. The "principles of laboratory animal care" (NIH Publication No. 85 – 23, revised 1996) were followed and permission to carry out the research was obtained from the Research Ethics Committee of MUST and approval of the study was obtained from Uganda National Council for Science and Technology with the registration number HS463ES.

Acute toxicity test

The median lethal dose (LD_{50}) of extracts was determined *in vivo* using the procedure described by Lorke (1983). In the first phase, nine rats were randomly divided into three groups of three rats each and each group received the extract at 10, 100 and 1000 mg/kg body weight orally via a feeding cannula. The rats were then observed for signs of adverse effects and mortality for 14 days.

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Since there were no deaths and side effects observed in the first phase, increased doses of the extract were administered in the second phase. In this phase, four rats were divided into 4 groups of 1 rat each and similarly treated at doses of 1000, 1600, 2900 and 5000 mg/kg, orally (Lorke, 1983). The animals were monitored for any sign of toxicity like stretching, rubbing of nose on the floor and wall of cage, change in body weight and mortality over a period of 14 days.

Sub-acute toxicity evaluation

Twenty four (24) animals between the weights of 120 and 150 g of both sexes were grouped into 4 groups of 6 animals per group. Groups I to III were given extract at 12.1, 24.1 and 48.2 mg/kg as lowest, medium and highest doses, respectively while group IV was given distilled water (0.2 mL) for 28 days. The body weight of each rat was assessed weekly during the dosing period.

On day 30, all the animals had their body weights taken before being anaesthetized and their organs, namely: liver, kidney, spleen, testis and ovaries (Carleton et al., 1980) were carefully removed and weighed in grams. The relative organ weight of each animal was then calculated as follows:

$$\text{Relative organ weight} = (\text{absolute organ weight} / \text{Body weight of rat}) \times 100$$

The blood was collected into heparinized BD Vacutainer® K2E (EDTA) for biochemical and hematological assays at the Clinical and Research Laboratory of MUST while the liver, kidney, brain, testis and spleen were removed for histopathological observation at the Department of Pathology of MUST.

Biochemical and hematological analysis

Each collected blood sample was mixed inside the vacutainer tubes using Blood Mixer (HOSPITEX) RM–500 and analyzed in an automated Haematology Analyzer; BECKMAN COULTER AC-T 5diff CP, Kraemer Blvd, Brea, USA (WBC Lyse, Fix, Hgb Lyse, Rinse) to determine the Pack Cell Volume (PCV), White Blood Cell (WBC), Red Blood Cell (RBC), Haemoglobin (HGB), Haematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Haemoglobin (MCH), Mean Corpuscular Haemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW), Platelet, Mean Platelet Volume (MPV), Neutrophils (NE), Lymphocytes (LY), Monocytes (MO), Eosinophils (EO) and Basophils (BA). These parameters were obtained for each blood sample using automated haematology analyzer at the Clinical and Research Laboratory of MUST. Biochemical parameters including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine were determined using commercial kits following standard procedures outlined by the producer, Randox Laboratories, UK.

Histopathological analysis

The organs were immediately kept in a bottle containing 10% Buffered Saline and left for 5 days (Carleton et al., 1980). Alcohol of different grades of 70, 80, 90% and absolute were used to enhance dehydration followed by clearing, using xylene as ante-medium agent to increase the refractive index for transparent visualization. These were conducted in an automated tissue processor (Leica TP1020). Paraffin wax was used for encapsulation of the tissue to provide rigid support for microtomy. Five microns thick section was made from paraffin wax-embedded tissue blocks with the aid of rotary microtome (Micron HM 325). Prior to staining, the sections were de-waxed with xylene, treated with graded alcohols and rinsed with distilled water. The nuclei were stained with an alum haematoxylin (Harris's) and rinsed with water to remove excess stain. A mixture of 1% hydrochloric acid in 70% alcohol was used to remove an excess stain from the tissues (differentiation) until only nuclei are revealed. The cell cytoplasm was stained with eosin and rinsed with water before it is dipped into xylene and mounted with resinous mountant on a microscope slide, covered with slip and examined under microscope at ×100 magnification.

Data analysis

All quantitative data was expressed as mean ± standard error of mean (SEM) while the variation in a set of data was analyzed through the one-way analysis of variance and the difference among the means was considered at 95% confidence level using the post-hoc method of Newman-Keuls using Graph pad Prism®5 software.

RESULTS

HPLC fingerprint of *D. steudneri* stem bark extract

The yield of the extract was 13.7%. The HPLC chromatogram of the aqueous extract of *D. steudneri* stem bark showed 15 characteristic signals as shown Figure 1. This chromatogram showed diagnostic peaks at the retention time of 4.1, 19.7 and 19.89 min which will guide in identifying and confirming any of this extract following the same process of extraction and same condition.

Acute toxicity study

The acute toxicity study of *D. steudneri* aqueous extract showed no significant changes in behavior, gastrointestinal effects, no evidence of convulsion during the observation period. There was no treatment related symptom or mortality observed after oral administration of the *D. steudneri* extract within 48 h and after 14 day post administration. Therefore, the LD_{50} of the extract is greater than 5 g/kg body weight.

Sub-acute toxicity test

The sub-acute toxicity study of *D. steudneri* Engl. extract was determined as per OECD guideline 407. All the animals that were given the plant extract daily at doses (12.1, 24.1 and 48.2 mg/kg) survived during the 28 days. There were no signs of toxicity and behavioral changes observed as compared to the control group.

The body weight of rats before, during and after treatment with the plant extract on daily oral administration of aqueous extract at doses of 12.1, 24.1

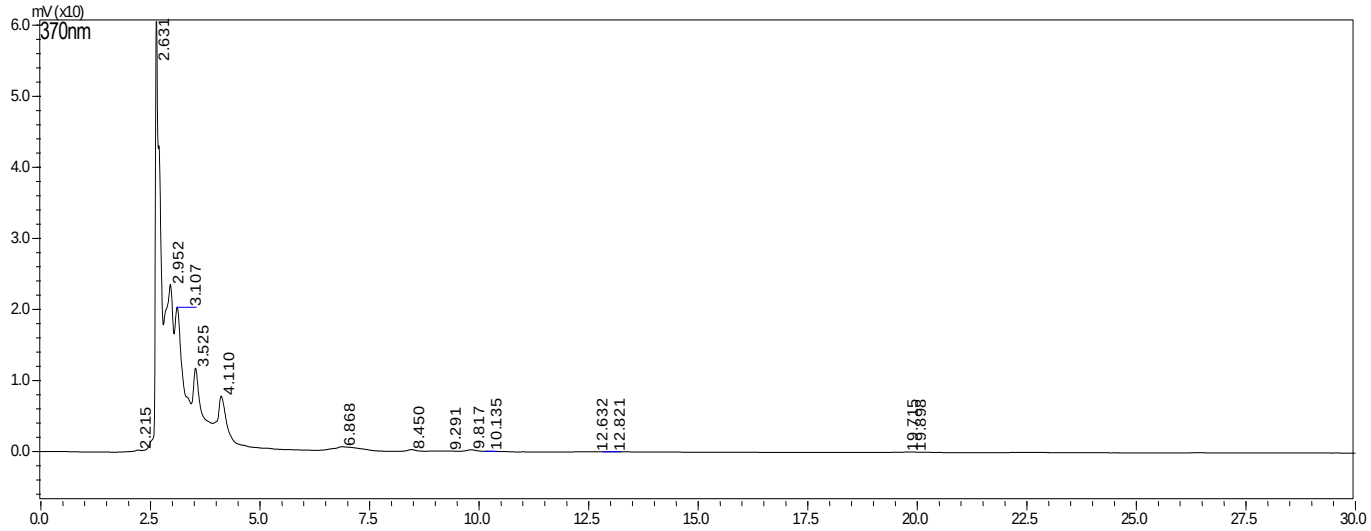

Figure 1. HPLC fingerprint of aqueous extract of *D. steudneri* stem bark.

Table 1. HPLC fingerprint signals obtained in aqueous extract of *D. steudneri* stem bark.

Peak#	Ret. time	Area	Height	Peak start	Peak end	Area%
1	2.215	3877	298	1.725	2.308	0.2543
2	2.631	463199	64197	2.308	2.792	30.3807
3	2.952	305327	23631	2.792	3.042	20.0260
4	3.107	288880	20409	3.042	3.433	18.9474
5	3.525	190487	11825	3.433	3.917	12.4938
6	4.110	231679	7906	3.917	14.883	15.1956
7	6.868	22281	552	6.283	7.867	1.4614
8	8.450	3594	244	8.117	8.767	0.2357
9	9.291	1486	83	9.133	9.467	0.0974
10	9.817	4924	264	9.550	10.108	0.3230
11	10.135	1386	79	10.108	10.475	0.0909
12	12.632	1983	63	12.067	12.783	0.1301
13	12.821	1347	62	12.783	13.208	0.0883
14	19.715	1612	78	19.233	19.758	0.1057
15	19.898	2587	84	19.833	20.825	0.1697

and 48.2 mg/kg for the 28 days did not cause any significant increase compared to the negative control (P > 0.05) for both sexes shown in Table 1.

The hematological parameters after the 28 days of administration showed a reduction in WBC which was not significant when compared with the negative control. Also, there was a dose-dependent decrease in RBC, HGB and HCT which were not significant (p>0.05) from the negative control shown in Table 2. However, MCV showed a significant increase (p<0.01) in the parameter at 24.1 mg/kg when compared with the negative control (Table 3).

Serum biochemical parameters examined after the 28-day administration had increase on AST (p<0.05) levels at all doses (12.1 - 48.2 mg/kg) which were not significant when compared with the negative control whereas at all doses administered (12.1 - 48.2 mg/kg), have significant increases in the creatinine (p< 0.001) and ALT levels (P < 0.01, 0.05, 0.05), respectively, compared to control indices (Table 4).

The reduction in the weight of kidney recorded among the tested groups was not significant when compared with the negative control. The liver showed an increase in weight among the male rats that was not significant

Table 2. Effects of aqueous extract of *Dracaena steudneri* Engl., stem bark on body weight of Wistar rats.

Group	Body weight (g/week)				
	W0	W1	W2	W3	W4
Famale					
Control (10 mL/kg)	200.00±7.64	228.20±17.24	228.20±17.24	195.00±6.03	222.10±9.21
12.1 mg/kg	200.70±8.37	196.7±7.86	192.30±6.98	199.40±7.87	201.70±8.21
24.1 mg/kg	201.70±13.17	200.00±10.15	197.00±9.07	200.00±8.08	198.50±9.005
48.2 mg/kg	219.00±13.75	223.00±17.58	219.00±15.95	221.00±15.95	226.70±15.90
Male					
Control(10 mL/kg)	200.00±7.64	228.20±17.24	207.30±12.72	195.00±6.03	222.10±9.21
12.1 mg/kg	227.70±22.67	224.30±20.28	230.00±20.53	233.30±20.95	236.70±21.28
24.1 mg/kg	242.00±7.81	224.30±8.76	233.30±7.70	235.00±8.08	238.00±8.39
48.2 mg/kg	239.70±22.75	232.30±19.63	243.30±23.95	245.30±23.95	250.70±23.50

Data was expressed as Mean ±SEM; n=6; (females and males), no significant difference between *D. steudneri* Engl., treatment groups and control groups ($p>0.05$).

Table 3. Hematological parameters in Wistar rats after a repeated administration of *D. steudneri* Engl. aqueous extract.

Parameter	Negative control	12.1 mg/kg	24.1 mg/kg	48.2 mg/kg
WBC ($\times10^3/mm^3$)	15.55±2.63	10.07±0.92	10.00±1.60	12.00±1.53
RBC ($\times10^{12}/L$)	8.23±0.39	8.16±0.33	8.12±0.28	7.98±0.34
HGB (g/dl)	15.46±0.57	15.33±0.60	15.17±0.47	14.55±0.57
HCT (%)	46.28±2.03	47.00±2.14	47.03±1.80	44.57±1.99
MCV (fl)	54.40±0.60	57.33±0.61*	58.00±0.52**	55.83±0.75
MCH (pg)	18.82±0.32	18.80±0.13	18.70±0.13	18.25±0.30
MCHC (g/dl)	34.68±0.23	32.63±0.37***	32.30±0.30***	32.67±0.31***
RDW (%)	12.26±0.30	11.40±0.44	11.78±0.33	12.05±0.40
PLT ($\times10^9/L$)	751.50±40.50	701.80± 20.04	697.30±47.38	684.70±48.20
MPV ($\times10^9/L$)	7.58±0.57	7.12±0.14	7.40±0.23	7.45±0.20
NE ($\times10^9/L$)	14.88±1.77	9.90±1.63	11.38±0.92	12.70±1.13
LY ($\times10^9/L$)	59.37±4.90	77.22±1.63**	74.08±1.70**	69.90±1.62
MO ($\times10^9/L$)	19.50±3.68	9.57±1.46*	11.28±2.10	14.60±1.90
EO ($\times10^9/L$)	4.88±1.56	2.23±0.48	2.40±0.72	2.10±0.80
BA ($\times10^9/L$)	1.37±0.16	1.10±0.12	0.90±0.10*	0.80±0.10**

Data is expressed as mean ±SEM; n=6; *$p<0.05$; **$p<0.01$; ***$p<0.001$. WBC=White Blood Cell; RBC=Red Blood Cell; HGB=Heamoglobin; HCT=Haematocrit; MCV=Mean Corpuscular Volume; MCH=Mean Corpuscular Haemoglobin; MCHC=Mean Corpuscular Haemoglobin Concentration; RDW=Red Cell Distribution Width; PLT=Platelet; MPV=Mean Platelet Volume; NE=Neutrophils; LY=Lymphocytes; MO=Monocytes; EO=Eosinophils; BA=Basophils.

compared to the negative control and also to the female groups. There was a significant reduction of the testis of male rats at 24.1 and 48.2 mg/kg (Table 5) for group of treated rats of both sexes and the control, and this was dose dependent.

Histopathology

The histological examinations on the kidney, liver, spleen, ovaries and testis did not show any deformation or any degeneration from the control groups. The histopathology of the liver showed morphologically intact hepatocytes among the groups examined. However, the kidney showed mucus congestion in the highest dose (48.2 mg/kg) while the glomeruli tubules were essentially intact. The spleen showed some impairment in the red pulp at the highest dose (48.2 mg/kg) while the white pulp was fully intact. The testicles showed normal spermatogenesis in the seminiferous tubules while the ovaries remained

Table 4. Liver and kidney function tests in rats after repeated administration of *D. Steudneri* Engl. aqueous extract.

Test	Negative control	12.1 mg/kg	24.1 mg/kg	48.2 mg/kg
CREAT	31.17±1.33	66.67±3.53***	62.83±3.12***	67.50±4.95***
ALT	57.98±6.63	120.7±11.97**	100.5±14.11*	111.8±12.77*
AST	165.2±24.25	216.6±20.37	193.7±11.22	215.4±24.58

Data is expressed as mean ±SEM; n=6; *p<0. 05; **p<0.01; ***p<0.001.

Table 5. Relative organ weight of Wistar rats after repeated administration of *D. steudneri* Engl., aqueous extract.

Organ	Negative control	12.1 mg/kg	24.1 mg/kg	48.2 mg/kg
Female				
Liver	4.72±0.09	4.61±0.10	4.40±0.28	4.12±0.17
Kidney	0.53±0.10	0.45±0.03	0.40±0.01	0.42±0.02
Spleen	0.64±0.04	0.50±0.02*	0.43±0.01*	0.54±0.06
Ovary	3.22±0.21	2.56±0.11	2.30±0.25	3.45±0.03
Male				
Liver	4.13±0.10	4.43±0.11	4.16±0.15	4.25±0.30
Kidney	0.80±0.04	0.54±0.13	0.39±0.03*	0.61±0.10
Spleen	0.50±0.04	0.43±0.02	0.51±0.05	0.46±0.02
Testis	2.86±0.15	1.68±0.34*	1.30±0.04**	1.40±0.11**

Data are expressed as Mean ±SEM; n=6; *p<0.01; **p<0.001

morphologically intact (Figures 2 to 4).

DISCUSSION

The extensive use of medicinal plants is increasing globally due to the factors considered as compared to conventional drugs like availability, affordability and fewer side effects that have increasingly led to their usage without the consideration of their safety profile (Karuiki and Njoroge, 2011). About 80% of the world population has been reported to depend directly on medicinal plants for their primary health care (WHO, 2002). The phytochemical compounds in these herbal medicines take an important role in therapeutic application and are responsible for their pharmacological activity. Likewise, these phytochemicals are also responsible for the toxicity in them, if not controlled. Therefore, it is important to carry out scientific research on the toxicity of these plant extracts containing different phytochemicals to establish their safe dose and therapeutic index (Adaramoye et al., 2008).

The acute toxicity of the aqueous extract of *D. steudneri* Engl. stem bark could be ranked in the class of lower toxic substances, as its LD_{50} was greater than 5 g/kg (OECD, 2001). There was no significant change in body weight in animals compared to the control after the 28 days of treatment which showed that the animals were normal during the treatment (Muhammad et al., 2011).

It was reported that the hematopoietic system is one of most targeted and sensitive targets of toxic compounds and is an important index of physiological and pathological changes in animals (Diallo et al., 2010). The hematological parameters between control and treated groups showed that the extract was not toxic. Though, there was a decrease in Lymphocytes, Basophils, Monocytes, and Mean Corpuscular Hemoglobin Concentration in extract treated, compared to control. This could be an indication for immune system compromise since the Lymphocytes were fluctuating and were the main effector cell of the immune system (Odeghe et al., 2012) and could be due to drug metabolism which can be reversed when the drug administration is stopped and this means that the *D. steudneri* extract might have compromised the immune system during the long term administration. At high doses, it is possible to have a decrease in the immune system which requires further exploration. There were no significant changes in the White Blood Cells which are known to be body defenders against toxic components (Agbor et al., 2005).

The relative weight of an organ is another criterion used in evaluating a damaged or affected organ (Rosidah et al., 2009). When animals are exposed to a toxic

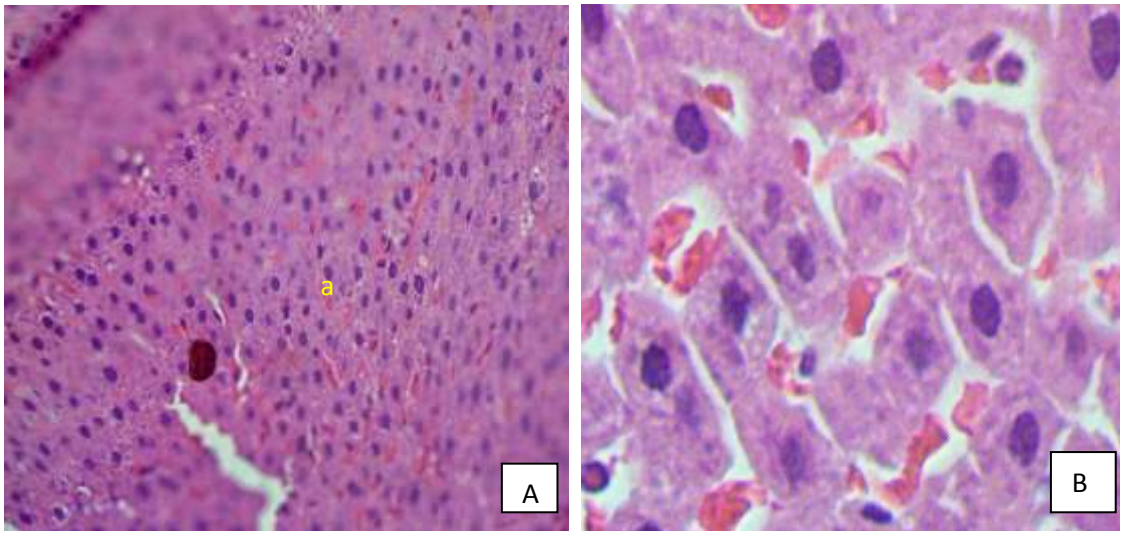

Figure 2. Histopathology of the liver of rats administered with distilled water (A) and extract at 48.2 mg/kg (B) after 28-day administration (H&E ×400).

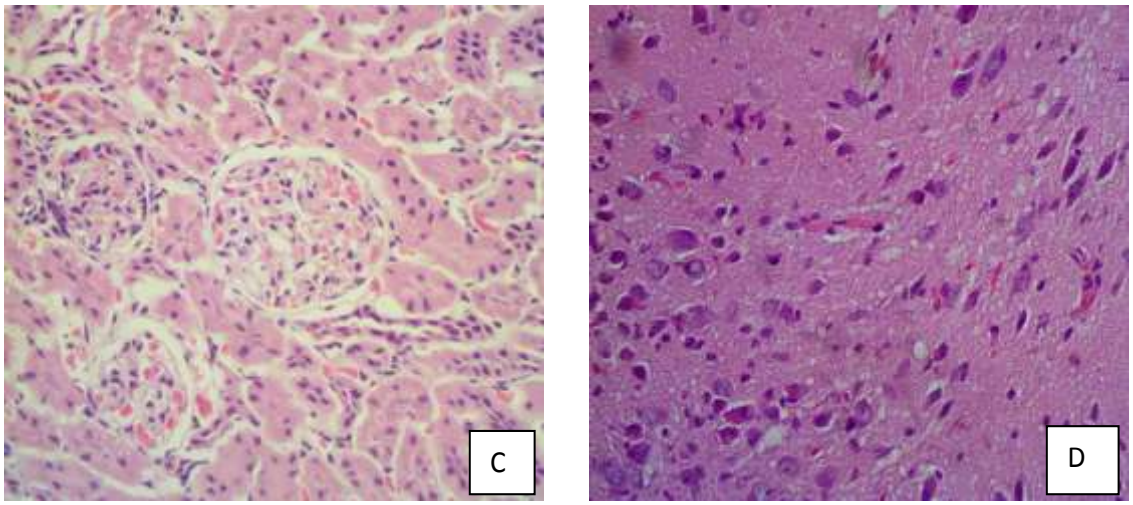

Figure 3. Histopathology of the kidney of rats administered with distilled water (C) and extract at 48.2 mg/kg (D) after 28-day administration (H&E ×400).

substance, there is potential functional impairment of target organs (Unuofin et al., 2018). When there is organ damage, the weight of the affected organ will vary as well as the relative organ weight. However, in this study, there were no significant differences detected (P>0.05) in the organ ratios of all tested doses compared to the control group.

Some herbal remedies could be toxic to the body depending on their usage/dosage and this toxicity of ingested herbal remedies is likely to affect the liver and kidneys because of the vital roles that they play in the body (Oshiomame et al., 2018).

The liver being the major organ used for detoxification, some herbal remedies have a high hepatotoxic effect on the liver (Frenzel and Teschke, 2016). Therefore, the evaluation of renal and hepatic function is of great importance to assess the toxicity profiles of drugs and plant extracts that they exert (Rahman et al., 2001). Alanine transaminase enzyme (ALT) is found primarily in the liver and is the most sensitive to liver damage hence the biomarker used to assess the liver functionality. There was an increase in ALT levels though not significant compared to the control but this slight increase could have been associated with the disruption of the hepatocytes observed at the highest dose (48.2 mg/kg) of *D. steudneri* aqueous extract administration. The

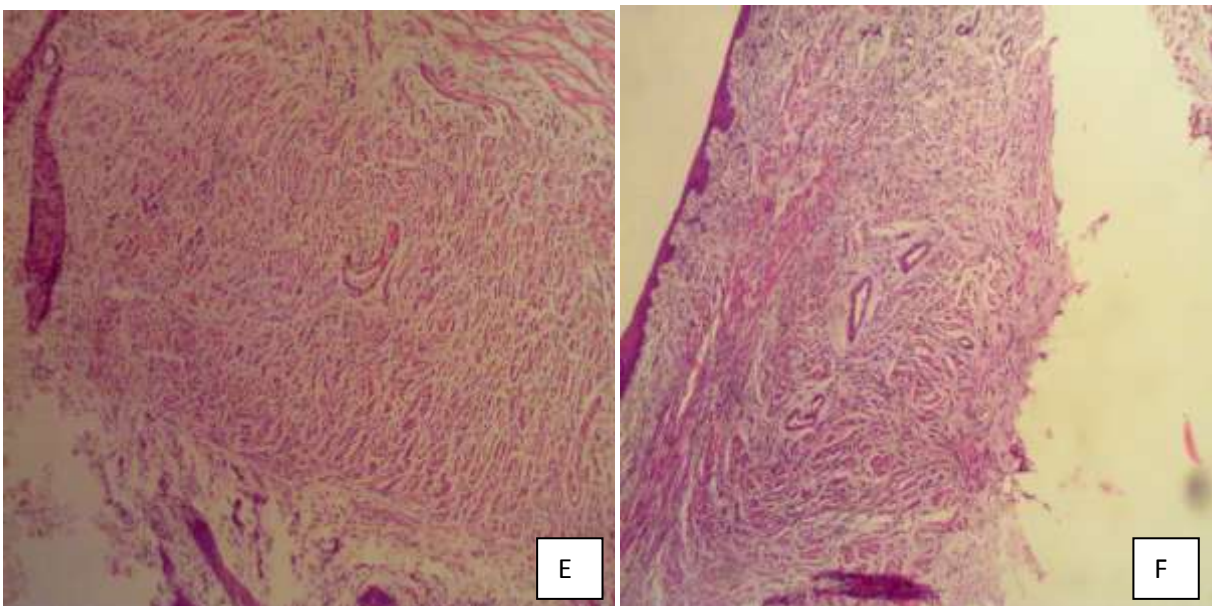

Figure 4. Histopathology of the ovary of rats after 28 days administration of distilled water (E) and extract at 48.2 mg/kg (F) (×100).

increase in creatinine levels were seen to be mild and does not suggest kidney damage (P<.001) as in Table 3. As reported by _Giannini et al. (2005) that the magnitude of aminotransferase alteration can be classified as “mild” (< 5 times the upper reference limit), “moderate” (5-10 times the upper reference limit) or “marked” (> 10 times the upper reference limit). The elevated levels in ALT and AST levels are indicators of liver damage or damage on other organs like the heart that also synthesizes them in small amounts or an indication in alteration in bile (Giannin et al., 2005). Creatinine that is an amino acid derived from Creatinine and is used to assess and diagnose kidney functionality. The elevated levels of creatinine are a biomarker for kidney damage (Anne-Sophie et al., 2018). Fetal cells were essentially normal compared to the normal control group.

Conclusion

The results of this study showed that *D. steudneri* Engl. stem bark is acutely safe since no mortality was reported up to 5000 mg/kg. Also, the extract did not lead to loss of appetite and body weight. However, the repeated dose showed deleterious effects in the liver and kidney with significant increase in serum ALT, and creatinine levels. Therefore, it could be concluded that the repeated dosing of the extract at higher dose may lead to hepatic and renal toxicity. Hence, considering the wide spread traditional use of this plant and the safety of the people, this plant should be used with caution in cases of increased and repeated dosages.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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