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Toxicological evaluation of *Commiphora swynnertonii* stem bark exudates on mice and rats

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Abstract

The aim of this study was to evaluate the safety of *Commiphora swynnertonii* stem bark exudates by determining its acute and sub-acute toxicity in mice and rats. The acute toxicity of exudates was administered to mice by oral administration of a single dose of tested concentrations and observed for 14 days. The doses were 500, 1000 and 3000mg/Kg body weight. The sub-acute toxicity test of the exudate was conducted on rats through a daily oral administration of various doses for 28 days. The doses were 250, 500 and 1000mg/Kg body weight. The physiological, behavioral and body weight change as well as relative weight of internal organs were subsequently recorded. Hematological, biochemical and histopathological parameters for rats used in the sub-acute toxicity assay were also measured at day 28. Results showed that, administration of up to 3000 mg/Kg body weight the *C. swynnertonii* exudates in mice did not result into any observable toxicity or mortality within the period of 14 days. Furthermore, the sub-acute toxicity test revealed that the exudates did not induce mortality neither behavioral nor physiological changes after 28 days. It was further observed that, the rat's body and relative internal organs weight as well as hematological, biochemical and histopathological parameters did not change as results of receive the doses for the whole period of the study. Therefore this study has revealed that *C. swynnertonii* stem bark exudates is safe for oral administration at low and moderate doses.

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Introduction

In recent years the use of medicinal plants as sources of alternative drugs and dietary supplement have increased in the developing countries (Bakari, 2012; Nagagi *et al*., 2016). The large population in these countries depends on medicinal plants as an alternative to modern drugs (Gautam & Goel, 2014). Due to the increase of diseases burden, disorders, side effects coupled with the costs of modern drugs, people in the developing countries switch to herbal remedies which are believed to be more safer and readily available (Alam *et al*., 2011). As a result, in the developing countries herbal medicines contribute about 80% of the human and animal health care (Bulus *et al*., 2011; Badarunisha *et al*., 2014; Mkangara *et al*., 2014).

Commiphora swynnertonii (*Burseracea*) is a small woody plant which can grow up the height of 2.5 meter (Van Wyk & Wink, 2004; Rahman *et al*., 2008). The plants is found in the arid and semi-arid environment and grows with tiny leaves and spiny (Paraskeva *et al*., 2008). *C. swynnertonii* has been reported to be used for the treatment of various human and animal diseases (Deepa *et al*., 2015; Baranitharan *et al*., 2016). Among human diseases, this plant species is used in the treatment of sexually transmitted diseases, ulcers and wounds (cut wounds and burn wounds), recalcitrant ulcers, and abscesses, swelling of legs, chesty cough and scabies (Kalala *et al*., 2014a). Previous pharmacological research have indicated that this plant species has higher antibacterial and antifungal properties (Musa, 2008; Rahman *et al*., 2008).

Furthermore, *C. swynnertonii* extracts have been reported to be used in the control of ectoparasite in livestock such as ticks, lice, bed bugs and mites (Kalala *et al*., 2014b; Mkangara *et al*., 2014). Despite of these numerous reports there is a limited scientific evidence on the safety of *C. swynnertonii* stem bark exudates, when administered to animals and humans. Therefore the aim of this study was to evaluate the *in vivo* safety of *C. swynnertonii* stem bark exudates using albino mice and rats.

Materials and methods

Plant materials

The exudates were collected from the stem bark of *C. swynnertonii* in Simanjiro District Arusha between June and October 2016. The *C. swynnertonii* plants were identified by botanist from Tropical Pesticide Research Institute (TPRI) Arusha Tanzania and its voucher specimen (CS 001) was deposited at Nelson Mandela African Institution of Science and Technology.

Preparation of the doses

Dimethyl Sulphoxide (DMSO) manufactured by Avantor Performance materials India Limited was used to prepare various concentrations. All concentrations were prepared in 10% DMSO in distilled water. For acute toxicity, the concentrations of 500, 1000 and 3000 mg/kg body weight were used while 250, 500 and 1000 mg/kg body weight were used for sub-acute toxicity.

Animals

Acute and sub-acute oral toxicity test was performed as per Organization for Economic Co-operation and Development number 407 guidelines (OECD, 2001). All experiments were carried out in accordance with ethical guidelines of the Sokoine University of Agriculture (SUA) Morogoro, Tanzania. Swiss albino mice and rats of both sexes and non-pregnant were randomly collected from SUA Morogoro, Tanzania. The age of mice and rats ranged between 8-12 weeks while weights of mice were between 23.8 and 35.4g and that of rats were 80.33 to 221g. All animals were housed in the wire marsh cages, supplied with synthetic diet grower marsh (Manufactured by Harsho Trading Co Ltd Moshi, Tanzania) and water *ad libitum*. In addition, room temperature was maintained at 28±5°C and the lighting was controlled to supply 12 hours of light and 12 hours of darkness for each 24 hours period. Before dosing, animals were acclimatized for 7 days and their body weight were determined.

Experimental design for acute toxicity

Sixteen mice were randomly assigned into a control and three treated groups each containing two males and two females. Animals were kept fasting overnight prior to dose administration.

Mice in control group were administered with 10% (DMSO) while treated groups received doses of 500, 1000 and 3000mg/kg body weight. The doses were given orally as a single dose through oral gavage.

Food and water were suspended for additional three hours post dose administration. After dose administration mice were observed individually during the first 30min, periodically during the first 24 hours (with special attention given during the first 4 hours), and daily thereafter for a period of 14 days. After the end of 14 days experimentation period, body weight measurements of each animal were recorded.

Experimental design for sub-acute toxicity

A total of 24 rats were randomly assigned into a control and three treated groups, each containing three males and three females.

The control group were given vehicle substance of 10% DMSO by oral route daily for a period of 28 days while treated groups administered dose of 250, 500 and 1000mg/kg body weight. After dose administration rats were observed individually during the first 30min, periodically during the first 24 hours (with special attention given during the first 4 hours), and daily thereafter for a period of 28 days. The body weights of animals were recorded after 28 days of experimentation period.

Blood analysis

At the end of the 28th sub-acute toxicity study, blood samples (approximately 1.3 ml) were collected in ethylene diamine tetra acetic acid (EDTA) vacutainer tube from orbital sinus to perform hematological tests in an ABX micros 60 automated hematology analyzer (manufactured by HORIBA ABX-USA).

Similarly blood samples (approximately 2ml) were collected in plain vacutainer tube and serum was obtained by centrifuging at 3000 rpm for 10min to perform biochemical tests in semi auto biochemistry analyzer (Uv 2800 spectrophotometer manufactured by Unico-USA).

Hematology assays

White blood cell (WBC), Red Blood cell (RBC), mean cell volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell (erythrocyte volume) Distribution Width (RDW), hemoglobin (Hb), Mean Platelet (thrombocyte) Volume (MPV), and Platelet distribution width (PDW) were evaluated for both control and treated groups of rats.

Biochemical assays

Glucose, cholesterol, total protein, albumin, triglycerides, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin were determined in all groups.

Histopathology

All the rats were anaesthetized and sacrificed to examine gross pathology of visceral organs. The internal organs such as liver, lungs, kidneys, spleen and heart were collected and weighed (OHAUS Scout pro SPG 202F, USA).

Additionally, relative organ weights of each animal in both groups was calculated. Histopathology examination of the internal organs was performed for high dose (1000mg/kg body weight) and control group animals. Tissues were fixed with neutral formalin 10% and embedded in paraffin. Thereafter, they were manually sectioned with a microtome to obtain 4-5 µm-thick paraffin sections. Dewaxed sections were then stained with Hematoxylin and Eosin (H&E) and left to dry for about 30 minutes. The histopathological slides were examined under the microscope (Optika B 350, Italy) for different histopathological lesions.

Statistical analysis

Data were analyzed using GENSTAT (version 10 of 2014) to obtain group means and standard error of the mean (SEM) for comparison between the control and treated groups. The significance differences were assessed by one way analysis of variance ANOVA and the significant differences within the group was considered at $p<0.05$

Results

Acute oral toxicity

No mortality and signs of toxicity were observed in both control and mice group treated with *C. swynnertonii* stem bark exudates at 3000mg/kg body weight during the 14 days observation period (Table 1). Additionally, there was a gradual increase in body weight of both control and treated mice (Table 2).

Sub-acute toxicity

There was no mortality observed in both the treated and control groups within 28 days of oral administration of *C. swynnertonii* exudates. General behavior and physiological activities of the rats were found to be normal throughout the study period. Both controls and treated groups were observed to be relatively healthy throughout the study.

Table 1. Effects of oral administration of *C. swynnertonii* stem bark exudates on physiological and behavior change in mice.

Parameter	Doses (mg/kg body weight)			
	Control	500	1000	3000
Eye lid closure	-	-	-	-
Difficulty in breathing	-	-	-	-
Change in skin	-	-	-	-
Eyes mucus membrane	-	-	-	-
Sleep	-	-	-	-
General weakness	-	-	-	-
Loss of appetite	-	-	-	-
Diarrhea	-	-	-	-
Excitement	-	-	-	-
Mortality	nm	nm	nm	nm

Keys: – = no physiological/behavior changes, + = observed physiological/behavior changes, nm = no mortality.

Table 2. Effects of oral administration of *C. swynnertonii* stem bark exudates on body weight (g) in mice.

Dose (mg/kg)	Sex	Mean weight at day 0	Mean weight at day 14	p- value
Control	M	31.26 ± 1.55	32.6 ± 2.17	0.587424
	F	27.4 ± 1.58	29.18 ± 1.32	0.228511
500	M	28 ± 1.82	29.64 ± 1.49	0.385250
	F	24.8 ± 1.72	26.2 ± 1.34	0.391518
1000	M	35.4 ± 1.35	37.57 ± 0.69	0.32142
	F	23.8 ± 1.76	25.44 ± 0.94	0.36085
3000	M	30.74 ± 1.5	32 ± 0	0.294342
	F	28 ± 2	29.26 ± 1.40	0.545162

Values are expressed as mean ± SEM, p< 0.05 values considered significant.

Body weight

There was gradual increase in body weight from day 0 to day 28 for both treated and control groups of rats. However, the increase in weights for both groups revealed no statistically significant difference (p>0.05) as shown in Table 3.

Relative organ weight

Results of relative organ weights of rats treated with *C. swynnertonii* exudates are shown in Table 4. In this study, there were significant differences (p<0.05) in relative weight of heart and lungs for female rats at doses of 250 and 1000mg/kg body weight respectively.

Table 3. Effects of oral administration of *C. swynnertonii* stem bark exudates on body weight (g) in rats.

Dose mg/kg	Sex	Mean weight (g) at day 0	Mean weight (g) at day 28	p- value
Control	M	221.67 ± 0.88	223.67 ± 11.84	0.753062
	F	102.33 ± 0.88	111.67 ± 0.88	0.102705
250	M	145.67 ± 9.53	180 ± 8.66	0.056006
	F	133 ± 2.3	153 ± 9.24	0.103604
500	M	170.67 ± 28	181.67 ± 19.34	0.762721
	F	133 ± 2.3	134 ± 5.20	0.153462
1000	M	168.67 ± 4.91	179 ± 3.46	0.160631
	F	80.33 ± 0.33	91.67 ± 3.76	0.139738

Values are expressed as mean ± SEM, p< 0.05 values considered significant.

Table 4. Effects of oral administration of *C. swynnertonii* stem bark exudates on internal organs in rats.

	Dose (mg/kg)	Kidney (g)	Liver (g)	Lungs (g)	Spleen (g)	Heart (g)
Male	Control	0.00393 ± 0.000928^{ab}	0.028 ± 0.00681^{a}	0.00543 ± 0.0014^{a}	0.00253 ± 0.000809^{a}	0.0039 ± 0.000601^{a}
	250	0.0067 ± 0.00055^{ab}	0.0400 ± 0.002^{ab}	0.0053 ± 0.000907^{a}	0.00348 ± 0.00136^{a}	0.0056 ± 0.000289^{ab}
	500	0.00567 ± 0.000611^{ab}	0.033 ± 0.00404^{ab}	0.00503 ± 0.00118^{a}	0.00361 ± 0.000647^{a}	0.00473 ± 0.00147^{ab}
	1000	0.005 ± 0.000503^{ab}	0.039 ± 0.00404^{ab}	0.0056 ± 0.000113^{a}	0.00314 ± 0.00093^{a}	0.0056 ± 0.000115^{ab}
Females	Control	0.00653 ± 0.00264^{ab}	0.045 ± 0.00551^{b}	0.00893 ± 0.0000881^{ab}	0.00421 ± 0.0011^{a}	0.00806 ± 0.00083^{c}
	250	0.0038 ± 0.000702^{a}	0.042 ± 0.00458^{b}	0.01317± 0.000809^{bc}	0.00459 ± 0.00033^{a}	0.00493 ± 0.00119^{ab}
	500	0.00427 ± 0.00101^{ab}	0.0437 ± 0.00318^{b}	0.01362 ± 0.00284^{bc}	0.00384 ± 0.000416^{a}	0.00677 ± 0.000667^{bc}
	1000	*0.00773 ± 0.00198^{b}*	*0.0437 ± 0.00176^{b}*	*0.01423 ± 0.0029^{c}*	*0.00296 ± 0.000463^{a}*	*0.00435 ± 0.000565^{ab}*

Values with the same superscript within the column means do not show statistically significant differences, mean ± SEM.

Hematological parameters

Results on hematological parameters are shown in Table 4. It was revealed that there were a significant difference ($p<0.05$) in MCV, MCH, MCHC, Hb, MPV and PDW for both control and treated groups of male rats treated with *C. swynnertonii* exudates at all doses of 250, 500 and 1000mg/kg body weight.

Biochemical parameters

Results on biochemical parameters in this study are shown in Table 5. It was revealed that there were a significant difference ($p<0.05$) in Total protein, AST, creatinine and bilirubin for both control and treated groups of male rats treated with *C. swynnertonii* exudates at all doses.

Table 5. Effects of oral administration of *C. swynnertonii* stem bark exudates on hematological parameters in rats.

Sex	Dose (mg/kg)	WBC (M/mm^3)	RBC M/mm^3)	MCV (fl)	MCH (pg)	MCHC (g/dl)	RDW	Hb (g/dl)	MPV (fl)	PDW
Male	Control	0.727± 0.22^{a}	4.87 ± 1.67^{a}	36.067 ± 14.2^{a}	27 ± 3.12^{a}	21.23 ± 7.33^{a}	7.617 ± 2.3^{a}	10.167 ± 3.72^{a}	7.4 ± 0^{a}	7.6 ± 0.12^{a}
	250	5 ± 1.98^{a}	5.87 ± 0.69^{a}	95.367 ± 20.5^{bc}	37.8 ± 8.89^{a}	59.467 ± 12.70^{bc}	23.47 ± 6.9^{a}	14.1 ± 0.98^{ab}	11.867± 2.5^{b}	14.67 ± 3.90^{b}
	500	5.26 ± 1.37^{a}	4.727±1.55^{a}	103.767 ± 26.2^{c}	73.13 ± 26.14^{b}	78.5 ± 23.04^{c}	30.13± 10.71^{a}	12.85 ± 2.22^{ab}	12.467± 2.6^{b}	15.2 ± 4.27^{a}
	1000	1.77 ± 0.28^{a}	6.62 ± 0.12^{a}	60.4 ± 0.64^{ab}	23.667 ± 0.20^{a}	39.267 ± 0.09^{ab}	12.467± 0.43^{a}	15.7 ± 0.40^{b}	7.467 ± 0.03^{a}	7 ± 0^{a}
Female	Control	2.823 ± 0.07^{a}	5.753± 0.25^{a}	59.1 ± 0.06^{ab}	23 ± 0.058^{a}	39.333 ± 0.38^{ab}	11.3 ± 0.208^{a}	13.067±0.58^{ab}	7.767 ± 0.03^{a}	7.667 ± 0.33^{a}
	250	2.697 ± 0.12^{a}	5.733 ± 0.2^{a}	58.7 ± 0.3^{ab}	22.433 ± 0.38^{a}	39.4 ± 0.45^{ab}	11.333±0.34^{a}	11 ± 1.16^{ab}	9 ± 0.577^{a}	7.767 ± 0.62^{a}
	500	2.757 ± 0.09^{a}	5.567±0.23^{a}	59.033 ± 0.09^{ab}	23.033 ± 0.52^{a}	39.366 ± 0.32^{ab}	11.3 ± 0.21^{a}	13.067± 0.55^{ab}	7.633 ± 0.15^{a}	7.533± 0.260^{a}
	1000	2.857 ± 0.08^{a}	5.773±0.29^{a}	59.167 ± 0.15^{ab}	23.3 ± 0.3^{a}	39.333 ± 0.49^{ab}	11.167±0.17^{a}	13.7 ± 0.40^{ab}	7.667 ± 0.08^{a}	7.267 ± 0.37^{a}

Values with the same superscript within the column means they are not show statistically significantly different ($p>0.05$), mean ± SEM, WBC=White blood cell, RBC=Red blood cells, MCV=Mean corpuscular volume, MCH=Mean concentration hemoglobin, MCHC=Mean corpuscular hemoglobin concentration, RDW=Red cell distribution width, Hb=Hemoglobin, MPV=Mean packed cell volume, PDW=Platelet distribution width.

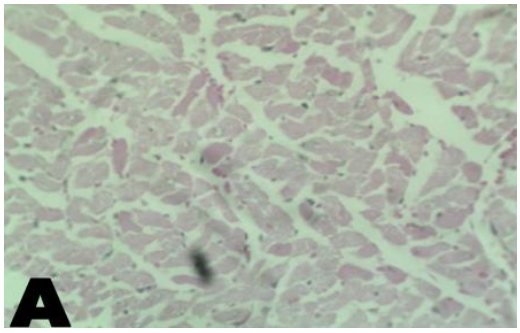
Table 6. Effects of oral administration of *C. swynnertonii* stem bark exudates on biochemical parameters in rats.

	Dose (mg/kg)	Glucose (mg/dl)	Cholesterol (mg/dl)	Total protein (mg/dl)	Albumin (mg/dl)	Triglycerides (mg/dl)	ALT (mg/dl)	ALP (mg/dl)	AST (mg/dl)	Creatinine (mg/dl)	Bilirubin (mg/dl)
Male	Control	56.99 ± 3.7^{a}	96.13±0.48^{ab}	7.24 ± 0.11^{b}	3.24±0.42^{ab}	94.02 ± 12.91^{a}	35.4 ± 3.4^{a}	59.55±10.76^{a}	72.53±2.21^{b}	25.71±5.67^{b}	0.89 ± 0.0088^{ab}
	250	45.77±2.89^{a}	105.21±5.59^{abc}	7.95±0.26^{c}	3.53± 0.05^{b}	11.1± 6.14^{a}	35.23±1.01^{a}	33.41±4.0^{a}	54.36±0.94^{a}	32.02±0.8^{b}	1.97 ± 0.026^{c}
	500	47.87±1.82^{a}	91.13 ± 6.62^{a}	7.89 ± 0.09^{c}	3.31± 0.42^{ab}	102.87±15.34^{a}	28.56±8.48^{a}	53.97±23.36^{a}	55.3±3.21^{a}	29.43±2.19^{b}	1.68 ± 0.03^{c}
	1000	60.28±8.40^{a}	109.35±2.28^{bc}	7.19±0.05^{ab}	2.6±0.02^{a}	94.61±6.31^{a}	30.43±4.31^{a}	73.57±19.92^{a}	73.17±5.89^{b}	14.11±5.67^{a}	0.92 ± 0.02^{b}
Female	Control	54.81±4.2^{a}	117.2±5.48^{c}	6.82±0.17^{a}	2.8±0.15^{ab}	94.07±6.72^{a}	31.12±5.22^{a}	46.81±6.7^{a}	48.07±0.58^{a}	28.73±1.23^{b}	0.88 ± 0.05^{ab}
	250	56.43±3.92^{a}	112.1±3.12b^{c}	7.13±0.09^{ab}	2.93±0.09^{ab}	93.13±5.75^{a}	31.13±4.36^{a}	44.5±7.43^{a}	69.6±4.35^{b}	25.18±2.52^{b}	0.81 ± 0.012^{a}
	500	48.47±2.15^{a}	114.67 ± 6.74^{c}	7.13±0.09^{ab}	3.0±0.02^{ab}	93.43±6.81^{a}	28.4±2.52^{a}	49.24±8.71^{a}	72.13±5.23^{b}	28.44±1.46^{b}	0.92 ± 0.02^{b}
	1000	51.23±6.59^{a}	104.98±3.66a^{bc}	7.10±0.06^{ab}	3.03±0.07^{ab}	102.59±2.34^{a}	30.4±4.84^{a}	41.77±7.80^{a}	68.7±4.35^{b}	26.21±2.27^{b}	0.87 ± 0.017^{ab}

Values with the same superscript within the column means do not show statistically significant differences ($p>0.05$), mean ± SEM, ALT=Alanine aminotransferase, ALP=Alkaline phosphatase, AST=Aspartate aminotransferase.

Histopathology findings

Histopathological findings of organs namely liver, heart, kidney, lungs and spleen in a group of rats treated with high dose (1000 mg/kg body weight) of *C. swynnertonii* exudates are shown in Fig. 1.



It was revealed that, there were no lesions observed in both control and treated animals.

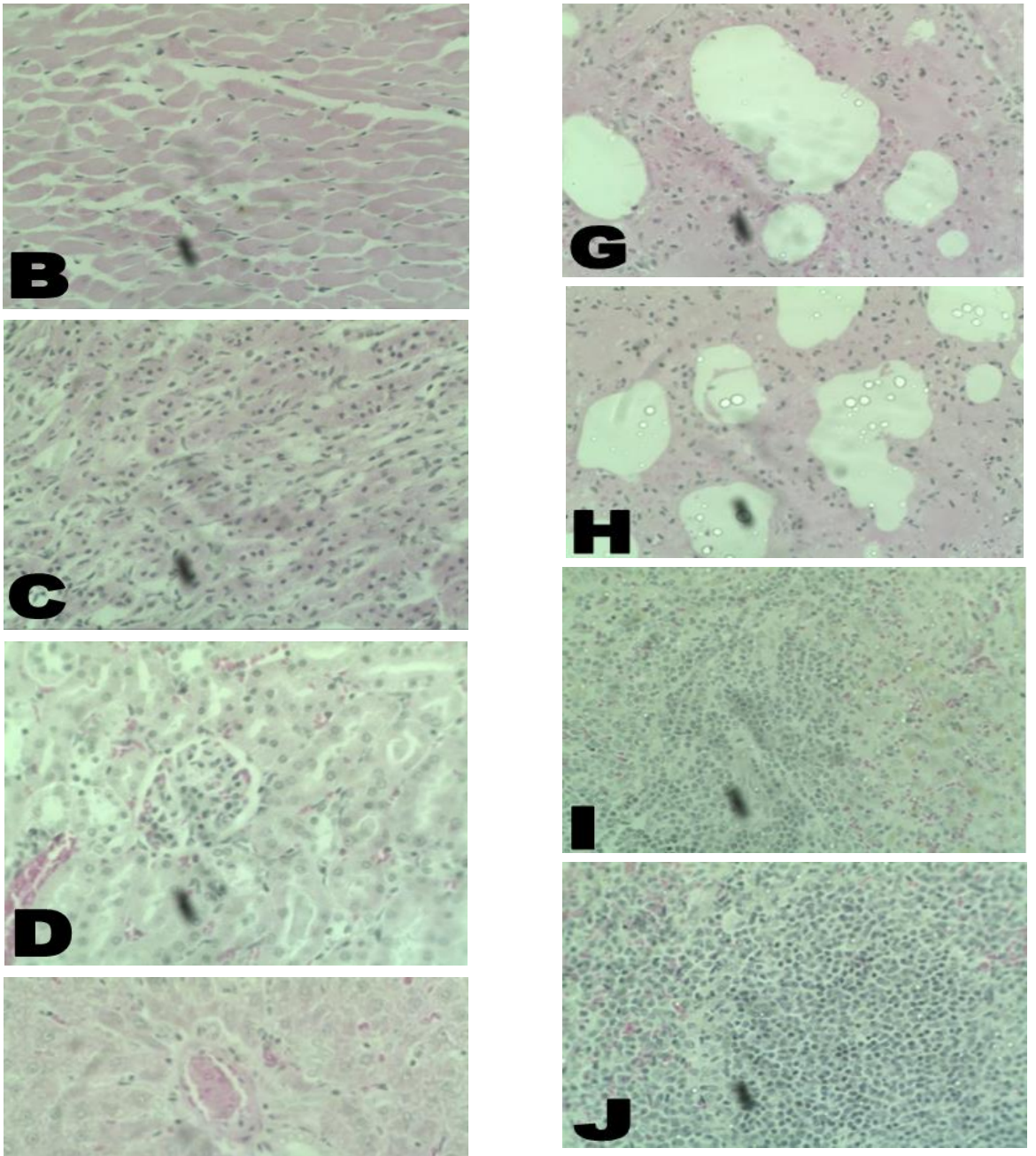


Fig. 1. Microscopic examination of stained section A:B control: treated heart, C:D control: treated kidney, E:F control: treated liver, G:H control: treated lungs, I:J control: treated spleen of rats at magnification 40X

Discussion

Medicinal plants have received greater attention as an alternative to clinical therapy and the demand for these remedies has currently increased (Sini *et al.*, 2010). The increase in number of users as opposed to the scarcity of scientific evidence on the safety of the medicinal plants, have been raised regarding toxicity and detrimental effects of these remedies (Alam *et al.*, 2011).

This study evaluated the acute and sub-acute toxicity of *C. swynnertonii* stem bark exudate using animal models.

The body weight was found to be increasing gradually from the beginning of the experiment to the end. The increase in weight is suggested to be contributed by improvement of nutrition as they were supplied synthetic grower marsh and water daily. The differences in the increase in weight of the animals treated with *C. swynnertonii* compared to the untreated group was statistically not significant ($p>0.05$). Further observation showed that, the exudate did not stimulate thyroid hormone which controls metabolism (Bakari, 2012; Mdegela *et al*., 2017).

Therefore it can be concluded that the stem bark exudate of *C. swynnertonii* did not influence animal weight gain or loss. However for the internal organs, there was no any changes in relative organ weight of the animals when treated and control groups were compared.

Hematology assessment parameter is important in determination of any adverse effect of toxins taken orally (Adeneye *et al*., 2006). Analysis of blood parameters therefore assist in evaluation of any changes in some hematological parameters such as WBC, RBC, MCH, MCHC, RDW, Hb, MPV, PDW and prediction for toxicity (Gautam & Goel, 2014). According to Ouedraogo *et al*., (2013) the hematological indices in animal is used to decide toxicity threat as the change in blood system had higher projecting values for human toxicity. Since the current study did not reveal any significant differences in hematological parameters for both control and treated animals with *C. swynnertonii* stem bark exudate, it can be therefore suggested that the plant exudate is safe for dermal and oral application.

In a routine health evaluation, monitoring of enzyme serum maker as biochemical changes is essential. For instance, there are several biochemical activities which occur in the liver including; metabolism, degradation and synthesis. These processes or activities play key roles in the detoxification of chemical compounds (Reddy *et al*., 2013).

Thus, in any toxicological study, it is very important to assess the liver and kidney enzymes functions as these organs play a major role in the metabolism and removal of foreign substances from the body.

The enzymes ALT and AST tend to be elevated whenever the conditions associated with toxicity prevails. ALT is an indicator of liver functions and biomarkers for toxicity predictions (Mukinda and Syce, 2007: Kripa *et al*., 2011). In this study, the analyses of the serum were carried out in order to evaluate if there is any damage of liver and kidney induced due to oral administration of *C. swynnertonii* stem bark exudates.

The observations indicated that, there was a significant difference in AST between animals treated with *C. swynnertonii* exudates and untreated group (control group) ($p<0.05$). There was significance difference in protein, creatinine and bilirubin observed between controls and treated male rats however the observed difference was found to be within the range. (Aleman *et al*., 2015).

This indicates that liver was functioning well even after administration of *C. swynnertonii* stem bark exudates. Furthermore, there was no significance difference in glucose and cholesterol level between control group and treated groups, hence *C. swynnertonii* exudates has no effects on lipids and carbohydrate metabolism. Since most foreign substances are eliminated from the body through kidney (renal excretion) hence it is important to examine the creatinine level as a determinant of kidney function (Diallo *et al*., 2010).

The study revealed that, there was no difference in level of creatinine among the treated and control groups. This therefore confirmed that the kidneys were not damaged by the *C. swynnertonii* exudates.

The structures of all organs was found to be normal, there was no observable change in morphology between treated and control group. Generally histopathology was in line with body weight and organ weight index. This study suggest that the *C. swynnertonii* exudates have got lower toxicity levels.

Conclusion

This study has shown that the *C. swynnertonii* exudate does not have severe toxicological effects as there was no observable changes in physiological behavior, body weight, and relative organ weight as well as hematological, biochemical and histopathological parameters. This study suggest that *C. swynnertonii* stem bark exudates is safe for oral or dermal applications at lower dosage, however further studies is recommended.

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