

Hepatotoxic and Nephrotoxic Effect of Ethanol Leaf Extract of *Scoparia Dulcis* (Linn) in Wistar Rats

Olubodun A. Adebisi, Danladi A. Ameh, Elewechi Onyike, and Dorcas B. James

ABSTRACT

Scoparia dulcis (Linn) is a widespread herbal medicine; it bears an enormous number of pharmacological activities. The present study was undertaken to find out the chronic toxicity profile of oral administration of *Scoparia dulcis* ethanol leaf extract (SDELE) on the liver and the kidney of wistar rats. The animals were grouped into four and administered varying doses of SDELE (100 mg/kg, 200 mg/kg, 400 mg/kg body weight and 0.2 ml distilled water respectively) for a period of fourteen weeks (100 days). The acute toxicity, body weight, relative organ weight, hematological parameters, biochemical markers for liver and kidney damage were monitored and histopathology of the liver and kidney of the rat were carried out. The LD₅₀ of SDELE was found to be 1131 mg/kg body weight. There was a significant ($p < 0.05$) reduction in weight of the rat administered 400 mg/kg and 200 mg/kg when compared with the control though there was no significant difference ($p > 0.05$) in the relative weight of the organs. There was also a significant increase ($p < 0.05$) in the lymphocytes, serum level of aspartate amino transferase (ASP), alanine amino transferase (ALT), alkali phosphatase (ALP), total protein, A/G ratio, creatinine, urea, uric acid, total cholesterol, triacylglycerol, low density lipoprotein cholesterol and potassium ions while there was a significant decrease in HDL-cholesterol and sodium ions in the animal group administered 400 mg/kg body weight of the extract. Histopathology of the liver and kidney revealed haemorrhage and vascular congestion at 200 mg/kg doses and renal damage at 400 mg/kg body weight doses respectively. However, there was no significant difference ($p > 0.05$) in any of the parameters studied in the group administered 100 mg/kg body weight dose when compared with the controlled group. Ethanol leaf extracts of *Scoparia dulcis* showed hepatotoxic and nephrotoxic tendencies and should be used with caution especially when employed in the treatment of chronic diseases.

Keywords: Chronic toxicity, Hepatotoxic, Nephrotoxic, *Scoparia dulcis* (Linn).

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I. INTRODUCTION

Scoparia dulcis (Linn) is a plant grown in many parts of the world. It is found in India, Brazil, Africa, and other tropical region of the world. The plant had been reported to be of use by traditional healers for the treatment of a vast array of disease conditions like bronchitis, diabetes, hemorrhoids, hepatitis, hypertension, inflammation, and stomach troubles. It can also serve as analgesic, antibacterial, antifungal, anti-diarrhoeal, anti-inflammatory, antiherpetic, antipyretic, antiseptic, anti-spasmodic, antiviral, cytotoxic, emollient, emmenagogue, febrifuge, and hepatoprotective [1]-[6], neuroprotective and anticholinergic [7]. The use of the whole plant *S. dulcis* for treatment of bite occasioned by the snake *B. asper* (Viperidae) in the province of Antioquia in Colombia has been reported [8]. The healers are said to administer the plant extracts to neutralize the toxins such as

phospholipase A2 present in the venom [9]. The plant is commonly known as *Sweet broom weed* and widely distributed in all the geopolitical zones of Nigeria. The plant had been listed as one of the Nigerian most patronized medicinal plants employed in the treatment of *diabetes mellitus*, cough, conjunctivitis, and gonorrhoea [10]. Among the Hausa people of Nigeria, *Scoparia dulcis* (Linn) is usually administered by traditional birth attendants and old women to primigravids (women who just delivered a baby) as part of post natal care to help flush and clean the women post partum blood flow. It is also being used as love charm and often chewed to secure favour from people in authority [11]. Reference [12] reported the heamatinic, immuno-stimulatory and antibacterial potential of the plant. Several studies had been carried out on the anti-diabetic potential of the plant in animal models using streptozotocin or alloxan [13]-[19]. Bioactive components of *Scoparia dulcis* were found to

include scoparic acid A, scoparic acid B [2], scopadulcic acid A and B, scopadulciol and scopadulin [1].

These studies support the claims of traditional use of the plant for the treatment of diabetes mellitus. However, in our literature survey no report was available on evaluation of this plant for its possible toxicity. The diseases treated using this herb can be classed into infectious or non-metabolic which require a short or medium term of treatment and metabolic diseases like diabetes mellitus which involve a long term (chronic) management. Therefore, we cannot talk of the safety of this plant without carrying out the chronic toxicity profiling of the plant. Hepatotoxicity is defined as injury to the liver or impairment of the liver function caused by exposure to xenobiotic such as drugs, food additives, alcohol, chlorinated solvents, peroxidized fatty acids, fungal toxins, radioactive isotopes, environmental toxicants, and even some medicinal plants [20]-[22]. Moreover, nephrotoxicity deals with damages done to the kidney by these substances. So, the present study was undertaken to evaluate possible toxicity of the ethanol leaf extract of *Scoparia dulcis* L to confirm its safety or otherwise on the liver and kidney in the management of chronic diseases which involve a long time of administration.

II. MATERIALS AND METHODS

A. Plant Materials and Extraction

The leaves of *Scoparia dulcis* was collected from Ahmadu Bello University Samaru campus, Zaria Nigeria and was authenticated at the Herbarium unit of Botany department of the University. The plant material was shade dried for two weeks and pulverized using a kitchen blender (Sonifer®, model SF-8028). The powdered leaf sample was cold macerated using 70% ethanol for seventy two hours after which the solvent was evaporated using Rotary Vacuum Evaporator (Hahn Vapor, HS-2005V, Hahnshin Scientific Co., Korea) to obtain the *Scoparia dulcis* Ethanol leaf extract (*SDELE*) used for this study.

B. Animals

Healthy adult male albino rats weighing 110 to 130 g were obtained from National Animal Production and Research Institute (NAPRI, Vom, Nigeria) were grouped and housed in cages under 12 hours light dark cycle at 34 ± 2 °C with free access to standard pellet diet and water *ad libitum*. The animals were allowed to acclimatize to the laboratory conditions for two weeks prior to the commencement of the experiment.

C. Chemicals

All chemicals and reagents used in this study are of analytical grade. Kits for estimation of biochemical parameters (Protein, Albumin, Creatinine, ALT, AST, and ALP) are product of RANDOX Laboratory Ltd. Ardmore United Kingdom.

D. Acute Toxicity Study

The toxicity test was carried out on albino rats (100–120 g) in accordance with the protocol devised by Reference [23]. On the first phase, animals were grouped into three of three rats per group and administered 10, 100 and 1000 mg/kg body

weight doses respectively of *SDELE* orally and monitored for twenty four hours for signs of toxicity like, tremor, restlessness, pyloerectile display, dizziness and death. In the second phase, another set of rats (one per group) were given oral dose of *SDELE* at 200, 400, 800 and 1600 mg/kg respectively and monitored for twenty four hours for signs of toxicity.

E. Experimental Design Chronic Toxicity

Albino rats were divided into four cages of five rats in each cage. They were placed on rat chow and allowed to drink water *ad libitum*. Group I was administered distilled water as the control while the remaining groups were administered specified doses of *SDELE* orally once a day for a period of fourteen weeks.

The treatments were as follows:

- Group I: Normal rats were treated with 0.2 ml distilled water.
- Group II: Normal rats treated with 100 mg/kg body weight dose of *SDELE*.
- Group III: Normal rats treated with 200 mg/kg body weight dose of *SDELE*.
- Group IV: Normal rats treated with 400 mg/kg body weight dose of *SDELE*.

F. Body Weight, Relative Organ Weight, Feed, and Fluid Intake

The body weights of animals in each group were recorded on weekly basis while the water and feed intake were recorded on daily basis all through the period of the experiment. At the end of fourteen weeks of extract administration, the animals were weighed, sacrificed using light anaesthesia, bled appropriately and quickly dissected to harvest the liver, spleen, kidney, heart, and the lungs. These organs were rinsed in saline solution blotted dry and weighed.

G. Haematological and Biochemical Analysis

Blood was collected on after the fourteen week duration by cardiac puncture into EDTA container for hematological estimation using auto Hematology Analyzer (Mindray, BC-2800) while blood for biochemical estimations were collected in plain specimen bottles and serum was obtained by centrifugation at 3000 rpm for 10 minutes. Kits (RANDOX Laboratory Ltd. Ardmore United Kingdom) were used for biochemical assay while Serum electrolytes (Sodium and Potassium ions) were estimated using spectrophotometric technique [24].

H. Histopathology

The animals were dissected after a light anesthesia. The liver and kidney were harvested and fixed in 10% formol saline. The fixed tissues were transferred to a graded series of ethanol and then cleared in xylene. Once cleared, the tissues were infiltrated in molten paraffin wax in the oven at 58 °C. Serial section of 5 micrometers thick were obtained from a solid block of tissue, cleared, fixed in clean slides, stained with Haematoxylin and Eosin stains, and examined with the light microscope [25].

I. Statistical Analysis

Results were expressed as mean \pm SD. All data was subjected to one-way analysis of variance (ANOVA) and

Tukey's post hoc test at 95% level of significance using MINITAB 17 statistical software.

III. RESULT

A. Acute Toxicity Test

The result of the acute toxicity test is shown in Table I. In the first phase of the experiment, there was mortality of one out of the three rats at 1000 mg/kg body weight dose. 200 mg/kg, 400 mg/kg, 800 mg/kg, and 1600 mg/kg body weight doses were tried with mortality observed only at 1600 mg/kg. The median lethal dose was estimated at 1100 mg/kg body weight.

TABLE I: ACUTE TOXICITY RESULT

Dose (mg/kg body weight)	Mortality Index*	LD ₅₀
Phase 1: 10	0/3	
100	0/3	
1000	2/3	
Phase 2: 200	0/1	
400	0/1	
800	0/1	
1600	1/1	$\sqrt{800 \times 1600} = 1131$

* Number of dead animal in the group
Total number of animals in the group

B. Effect of the Different Doses of SDELE on the Fluid and Feed Consumption in Normal Rats

The feed and fluid intake pattern of rats in the chronic toxicity study of ethanol leaf extracts of *S. dulcis* (SDELE) in rats is shown in Fig. 1. There was no significant ($p > 0.05$) difference in the food intake (g/100 g rat/day) in each of the treatment group when compared to the control. All the treatment groups exhibited the same pattern of food consumption. However, the groups treated with 100, 200 and 400 mg/kg body weight of SDELE elicited fluid intake propensity in a dose dependent manner.

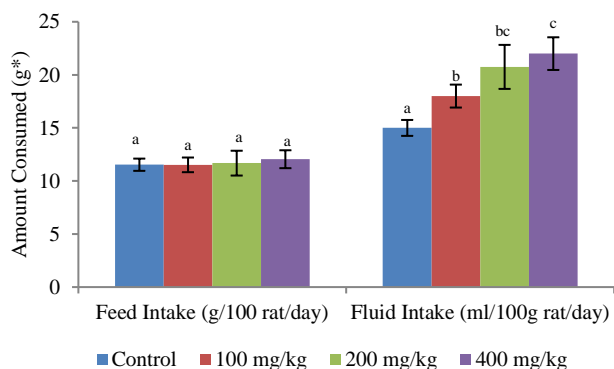


Fig.1. Effect of administration of SDELE on Feed and Fluid intake in normal rats for fourteen weeks.

^{a-c} Values with different letter for a given parameter are significantly ($p < 0.05$) different from the other group. * Density of water is 1 g/ml.

C. Effect of the Different Doses on Body and Relative Organ Weight upon Chronic Administration

The change in weight of rat administered 100 mg/kg, 200 mg/kg and 400 mg/kg of SDELE is shown in Fig. 2. The group administered 400 mg/kg body weight of SDELE shows a significant ($p < 0.05$) reduction in mean weight when compared with the control and other groups as from the

eleventh week while significant ($p < 0.05$) reduction in mean weight was noticed in the group treated with 200 mg/kg body weight dose at the thirteenth week. However, the 100 mg/kg dose of the leaf and stem extract of *S. dulcis* showed a similar trend in weight gained as the control group. Furthermore, there was a significant ($p < 0.05$) increase in the relative organ weight of the liver and heart tissues in the rat group administered 400 mg/kg body weight dose of SDELE (Table II) while there was no effect of the chronic administration of the extract on the relative organ weight of the spleen, kidney and lungs at 100 mg/kg, 200 mg/kg, and 400 mg/kg of SDELE.

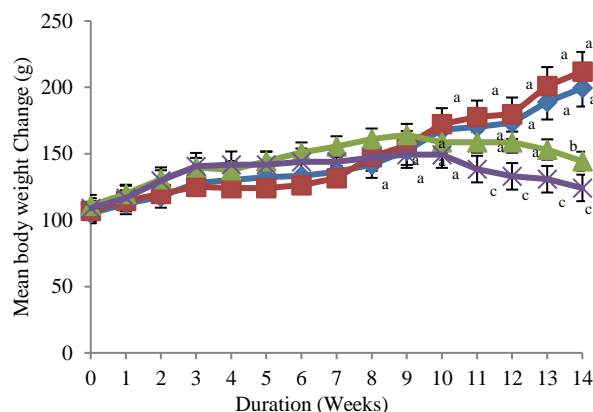


Fig.2. Effect of administration of SDELE on mean weight change of rats for fourteen weeks.

^{a-c} Values with different letters near the lines for a given week are significantly ($p < 0.05$) different from each other group of animal.

D. Effect of SDELE on Haematological Parameter upon Chronic Administration in Rats

The leaf extract of *S. dulcis* elicited significant ($p < 0.05$) increase in the percentage of the lymphocytes in rat groups administered 200 and 400 mg/kg body weight doses of the extracts (Table III). There was no significant ($p > 0.05$) difference in every other haematological parameter of the rat groups treated with the different doses of the extract.

E. Effect of Different Doses of SDELE on Liver Function upon Chronic Administration

The extract SDELE at 400 mg/kg body weight dose caused a significant ($p < 0.05$) increase in the concentration of total protein, the serum level of albumin, A/G, bilirubin (total and direct), alkaline phosphatase, alanine amino transferases, and aspartate amino transferases when compared with the control group after fourteen weeks of administration (Table IV).

F. Effect of the Different Doses on Kidney Function upon Chronic Administration

The Ethanol leaf extract of *Scoparia dulcis* (Linn) caused a very significant ($p < 0.05$) increase in the blood urea, creatinine and potassium levels at 200 mg/kg and 400 mg/kg body weight while the extract also caused a significant ($p < 0.05$) reduction in serum concentration of sodium at these dosage levels. The extract however did not show any effect different with the control group upon administration at 100 mg/kg dose level (Table IV).

TABLE II: EFFECT OF ETHANOL LEAF AND STEM EXTRACT OF *S. DULCIS* ON RELATIVE ORGAN WEIGHT IN THE CHRONIC TOXICITY STUDY IN RATS

Treatment	Spleen	Liver	Kidneys (g/100 g)	Lung	Heart
Normal Control	0.30 ± 0.05 ^a	3.36 ± 0.30 ^a	0.43 ± 0.05 ^a	0.79 ± 0.17 ^a	0.42 ± 0.05 ^a
Normal Rat+SDELE (100 mg/kg)	0.31 ± 0.06 ^a	3.45 ± 0.27 ^a	0.42 ± 0.05 ^a	0.83 ± 0.25 ^a	0.40 ± 0.04 ^a
Normal Rat+SDELE (200 mg/kg)	0.33 ± 0.04 ^a	3.79 ± 0.38 ^{ab}	0.42 ± 0.05 ^a	0.99 ± 0.16 ^a	0.42 ± 0.04 ^a
Normal Rat+SDELE (400 mg/kg)	0.37 ± 0.07 ^a	3.98 ± 0.26 ^b	0.39 ± 0.06 ^a	0.81 ± 0.16 ^a	0.52 ± 0.03 ^b

^{a-b}Values expressed as Mean ± SD of five animals with different letters along a column are significantly ($p < 0.05$) different from each other group of animals. SDELE means *S. dulcis* ethanol leaf extract.

TABLE III: EFFECT OF ETHANOL LEAF EXTRACT OF *S. DULCIS* ON HAEMATOLOGICAL PARAMETERS IN THE CHRONIC TOXICITY STUDY IN RATS

Parameters	Normal Control	Normal Rats	Normal Rats	Normal Rats
		+Extract (100 mg/kg)	+Extract (200 mg/kg)	+Extract (400 mg/kg)
Red blood cell ($\times 10^6/\mu\text{l}$)	4.87 ± 0.25 ^a	4.97 ± 0.25 ^a	4.90 ± 0.44 ^a	5.00 ± 0.51 ^a
Haemoglobin (g/dl)	13.50 ± 3.44 ^a	13.37 ± 2.87 ^a	13.83 ± 1.37 ^a	15.72 ± 1.56 ^a
Haematocrit (%)	40.91 ± 5.26 ^a	40.33 ± 7.62 ^a	41.88 ± 6.04 ^a	47.64 ± 4.62 ^a
Mean Corpuscular Volume (fl)	8.4 ± 0.46 ^a	8.11 ± 0.42 ^a	8.55 ± 0.44 ^a	9.50 ± 0.51 ^a
Mean Corpuscular Haemoglobin (pg)	27.72 ± 6.08 ^a	26.90 ± 2.76 ^a	28.22 ± 6.43 ^a	31.44 ± 8.69 ^a
Mean Corpuscular Haemoglobin Concentration (g/dl)	33.00 ± 0.00 ^a	33.07 ± 0.11 ^a	33.02 ± 0.00 ^a	33.00 ± 0.00 ^a
Platelet ($\times 10^3/\mu\text{l}$)	139.33 ± 48.06 ^a	144.67 ± 17.47 ^a	170.00 ± 17.32 ^a	182.00 ± 3.46 ^a
White blood cell ($\times 10^3/\mu\text{l}$)	3.13 ± 1.55 ^a	6.33 ± 2.31 ^a	6.17 ± 1.76 ^a	4.13 ± 3.51 ^a
Neutrophil (%)	54.65 ± 0.58 ^a	54.33 ± 3.06 ^a	53.34 ± 3.57 ^a	52.33 ± 2.83 ^a
Lymphocyte (%)	42.63 ± 0.57 ^a	42.67 ± 1.05 ^a	45.32 ± 0.58 ^b	46.00 ± 1.00 ^b
Monocytes (%)	1.67 ± 0.58 ^a	1.63 ± 0.62 ^a	1.33 ± 0.29 ^a	1.00 ± 0.10 ^a
Eosinophil (%)	1.00 ± 0.10 ^a	1.33 ± 0.23 ^a	1.00 ± 0.10 ^a	0.67 ± 0.58 ^a
Basophil (%)	0.00 ± 0.00 ^a	0.00 ± 0.00 ^a	0.00 ± 0.00 ^a	0.00 ± 0.00 ^a

^{a-b}Values expressed as Mean ± SD of five animals. Values with different letters along a row are significantly ($p < 0.05$) different from each other.

TABLE IV: EFFECT OF ETHANOL LEAF EXTRACT OF *S. DULCIS* ON BLOOD BIOCHEMICAL PARAMETERS IN THE CHRONIC TOXICITY STUDY IN RATS

Parameter	Normal Control	Normal Rats	Normal Rats	Normal Rats
		+ Extract (100 mg/kg)	+ Extract (200 mg/kg)	+ Extract (400 mg/kg)
Total Protein (g/L)	65.33 ± 3.44 ^a	65.75 ± 4.93 ^a	68.33 ± 4.31 ^a	74.93 ± 5.62 ^b
Albumin (g/L)	36.99 ± 3.11 ^a	37.39 ± 2.36 ^a	38.92 ± 1.07 ^a	44.92 ± 3.50 ^b
Albumin/Globulin	1.31 ± 0.12 ^a	1.34 ± 0.18 ^a	1.34 ± 0.13 ^{ab}	1.50 ± 0.06 ^b
Total Bilirubin (mmol/L)	2.74 ± 0.27 ^a	2.87 ± 0.70 ^a	3.07 ± 0.60 ^a	4.61 ± 0.70 ^b
Direct Bilirubin (mmol/L)	1.35 ± 0.11 ^a	1.37 ± 0.04 ^a	1.51 ± 0.29 ^a	2.44 ± 0.45 ^b
Urea (mmol/L)	5.91 ± 0.13 ^a	6.24 ± 0.64 ^a	10.05 ± 0.78 ^b	10.35 ± 0.96 ^b
Creatinine (mmol/L)	51.56 ± 2.34 ^a	50.40 ± 1.81 ^a	57.88 ± 5.72 ^{ab}	61.42 ± 5.53 ^b
Alkaline Phosphatase (U/L)	61.28 ± 3.92 ^a	66.78 ± 6.09 ^{ab}	79.78 ± 11.75 ^b	118.28 ± 14.91 ^c
Alanine aminotransferase (U/l)	33.40 ± 6.40 ^a	35.71 ± 3.86 ^a	48.67 ± 6.47 ^b	61.45 ± 6.55 ^b
Aspartate aminotransferase (U/l)	80.22 ± 2.49 ^a	79.40 ± 3.98 ^a	88.88 ± 3.12 ^b	92.40 ± 3.62 ^b
Sodium Ion (mmol/L)	140.20 ± 3.19 ^a	139.00 ± 2.49 ^a	139.80 ± 1.92 ^a	131.80 ± 6.30 ^b
Potassium Ion (mmol/L)	4.02 ± 0.31 ^a	4.06 ± 0.32 ^a	4.58 ± 0.16 ^b	5.30 ± 0.37 ^c

^{a-d}Values expressed as Mean ± SD of five animals. Values with different letters along a row are significantly ($p < 0.05$) different from each other.

G. Effect of Different Doses of SDELE on Histo-Architecture of the Liver and Kidney

Liver and kidney of rat treated with 100 mg/kg body weight dose of extract showed no remarkable pathology when compared to the liver from the control group. However, the liver from the group of rats administered 200 mg/kg body weight dose of extract for fourteen weeks showed mild haemorrhage (Plate 1c) while the liver architecture from the 400 mg/kg body weight dose group showed a vast area of haemorrhage (Plate 1d). Moreover, the kidney of rat administered 200 mg/kg body weight dose of extract showed areas of haemorrhage and vascular congestion (Plate 2c) while the architecture of kidney of rat administered 400 mg/kg body weight dose for a period of fourteen weeks revealed haemorrhage and renal damage (Plate 2d).

IV. DISCUSSION

Medicinal plants are very good sources of remedy for treating a vast array of disease conditions. However, studies had proved the potential danger of toxicity of these plants' extract on the organs in experimental animals [26]-[28]. The toxicity may arise from inappropriate use (usually an overdose), inappropriate identification of the plant material,

or be related to the presence of specific hepatotoxic and nephrotoxic compounds in the plant material.

The animal groups administered the extracts manifested more food consumption but same pattern of water consumption when compared with the control. The significant ($p < 0.05$) increase in the food consumption pattern of the treated groups may signify the appetite stimulatory potential of these extracts. Some appetite stimulatory plant extracts had been documented in the literature [29]-[31]. Food is known to supply nutrients needed for energy, growth, and maintenance of the entire body system. The more the quantity of the nutrients through food supplies, the more health, activity, and body mass of the subjects under a normal physiological condition. However, weight gain decreases were significantly ($p < 0.05$) noticeable as from the eleventh week at 200 and 400 mg/kg of SDELE administration. The reduction in weight gained of the groups administered higher doses of extract despite the high food consumption rate is an indication that food could no longer be converted for growth appropriately as from the eleventh week for SDELE. This could be adduced to the possibility of toxicity of the dosage of the extract at these periods which might have led to damages to internal tissues and organs and thus need to go through healing cycle. The nutrients that might have been employed in building body mass would have to be employed

in replacement of the affected cells. It could therefore be inferred that administration of the leaf extract of *S. dulcis* at 200 and 400 mg/kg body weight may be safe until the

eleventh week. Generally, the leaf and stem extract of these study plants are safe at 200 and 400 mg/kg body weight administration on sub-chronic level.

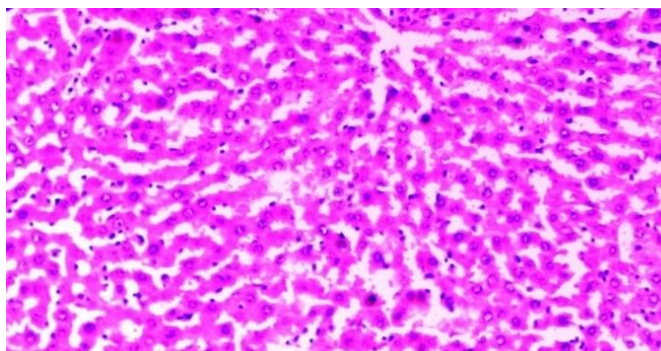


Plate 1a. Normal liver architecture (H & E. ×100).

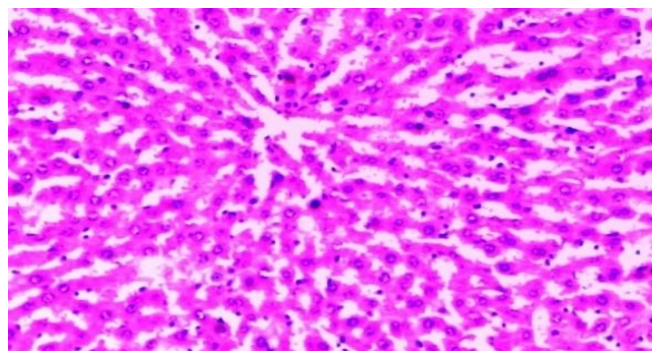


Plate 1b. Liver, 100 mg/kg (H & E. ×100).

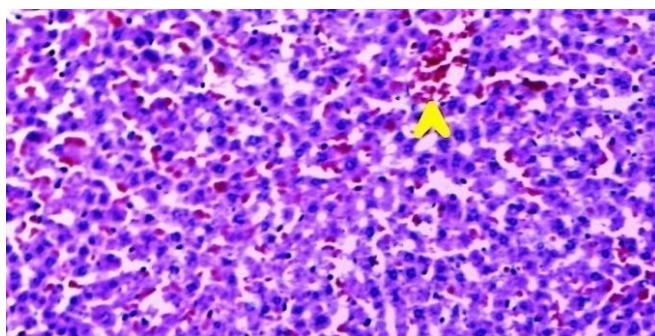


Plate 1c. Liver, 200 mg/kg (H & E. ×100).

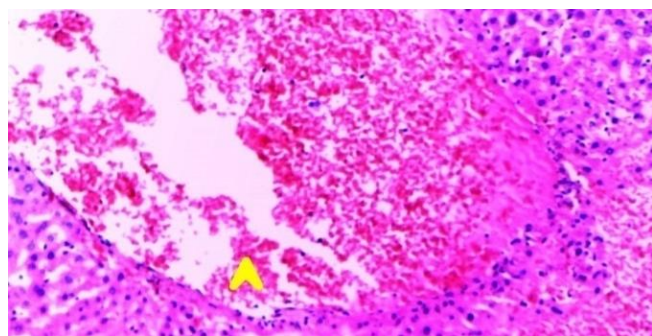


Plate 1d. Liver, 400 mg/kg (H & E. ×100).

Plates 1a-d: Photomicrographs of: (a) the liver of a normal control rat; (b) liver of rats administered 100 mg/kg dose of *Scoparia dulcis* ethanol leaf extract showing intact tissue; (c) liver of rat administered 200 mg/kg dose of *Scoparia dulcis* showing areas of mild haemorrhage (arrowed); (d) rat liver administered 400 mg/kg *Scoparia dulcis* leaf extract showing vast area of haemorrhage (arrowed) (H & E. ×100).

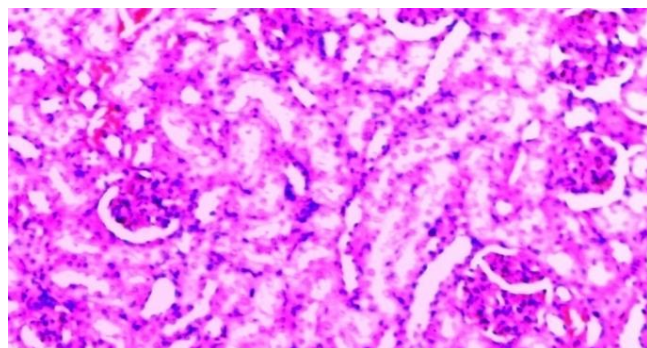


Plate 2a. Normal kidney architecture (H & E. ×100).

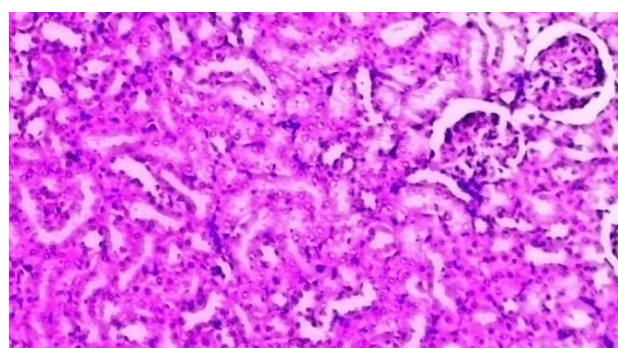


Plate 2b. Kidney, 100 mg/kg (H & E. ×100).

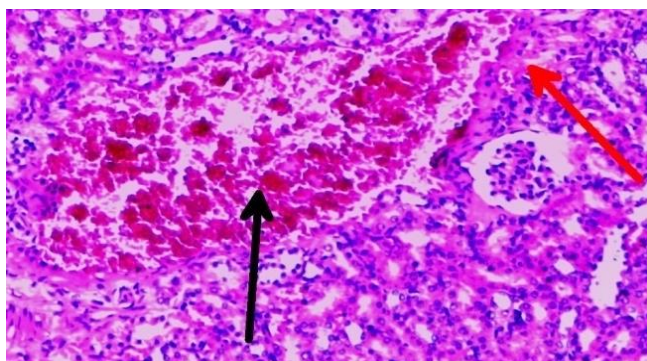


Plate 2c. Kidney, 200 mg/kg (H & E. ×100).

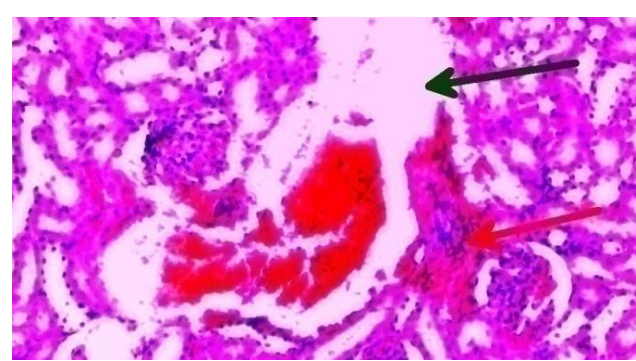


Plate 2d. Kidney, 400 mg/kg (H & E. ×100).

Plate 2a-d. Photomicrographs of: (a) the kidney of a normal control rat showing unremarkable kidney with the cortex containing glomeruli and medullary renal tubules; (b) the kidney of rat administered 100 mg/kg leaf extract of *Scoparia dulcis* showing intact tissue; (c) the kidney of rat administered 200 mg/kg leaf extract of *Scoparia dulcis* showing areas of haemorrhage (arrowed) and vascular congestion (arrowed); (d) the kidney of rat administered 400 mg/kg leaf extract of *Scoparia dulcis* showing areas of haemorrhage and renal damage (arrowed).

The significant ($p < 0.05$) increase in the relative weight (hypertrophy) of the liver and heart in the group administered 400 mg/kg body weight dosage of *S. dulcis* ethanol suggests the possibility of toxicity of these extracts at 400 mg/kg body weight dose. Hypertrophy may be good if it is physiological, when characterized by normal cellular growth (increase in cell size but not cell number) and enhanced function. Hypertrophy is caused by hormonal stimulation, inflammation and overload of the organ concerned as some cases when there is increased quantity of blood in the capillaries of, and retarded circulation in the affected organ.

Assessment of haematological parameters can be used to determine haematopoietic and haematinic related functions of an extract or compound. They can also be used to determine the extent of deleterious effect foreign compounds including plant extracts can exert on the blood constituents of an animal [32]. Such toxicity testing is relevant to risk evaluation as changes in the haematological system had been reported to have higher predictive value for human toxicity when data are translated from animal studies [33]. It can also be used to explain blood relating functions of chemical compound or plant extracts. The differential white blood counts revealed significant ($p < 0.05$) increase in the level of lymphocytes by animal groups administered 200 and 400 mg/kg body weight doses of SDELE. The lymphocyte is the main effector cell of the immune system [34]. The observed dose dependent increase in this parameter may likely be an indication that SDELE may exert serious challenge on the immune system of the treated animals at the 200 and 400 mg/kg body weight dose levels. The 100 mg/kg dose of this extract (SDELE) did not pose challenge on the immune apparatus of the animals as indicated by the non-significant ($p > 0.05$) difference in the level of their lymphocytes when compared with the control group.

The liver and kidney are two major organs in the mammalian body central to many metabolic transformations taking place in the body. The liver is saddled with the functions of detoxification, excretion of bile, storage of glycogen and vitamins, manufacture of protein (fibrinogen, albumin, and globulin), synthesis of blood clotting factors (fibrinogen, prothrombin, factor V, VII, IX, X and XI), synthesis of cholesterol, phospholipid, endogenous triglycerides, and lipoproteins (lipid metabolism) and removal of worn-out cells and microorganism through phagocytosis by the Kupfer cells [35], [36]. Where and when there is an attack or damage to this robust organ, there is tendency of compromise of one or more of these functions thereby leading to derangement of metabolic processes with devastating effect on the whole system which could culminate in complications and eventually death. Administration of SDELE at 200 mg/kg and 400 mg/kg body weight doses for fourteen weeks causes a tremendous increase in the serum level of bilirubin, ALP, ALT, and albumin. Bilirubin is mainly formed from the breakdown of haemoglobin in the cells of the liver, spleen, and bone marrow. The haeme is removed and the porphyrin of the globin part is converted to biliverdin which is reduced to bilirubin. The bilirubin is attached to albumin making it insoluble and cannot be excreted by the kidney. It is found in this form and referred to as unconjugated bilirubin. Glucuronic acid in the liver could conjugate with bilirubin

however making it soluble and excretable by the kidney (conjugated bilirubin). In situation of diminished function of the liver cells as in damage, conjugated bilirubin became accumulated and found in the blood in high concentration as we have in this study. Hence the extract could have caused damage to the liver at 200 and 400 mg/kg body weight dose level as seen in high concentration of bilirubin in the concerned groups. Hyperproteinemia observed in the serum of the group is an indication of chronic liver disease and nephrotic syndrome [37]. This may be a pointer that the extract is not friendly to the liver at 400 mg/kg body weight dose. ALP, AST, and ALT concentration are often used as biomarkers of hepatic damage [38]. In the present study we found a significantly higher activities of these enzymes in the serum of rats administered 200 and 400 mg/kg dose levels of SDELE. This is also an indication of possible damage to liver by this extract at these doses.

The kidney is the major organ responsible for excretion of toxins and their metabolites, maintenance of blood pH, water and electrolyte balance in the body, filtration, production of erythropoietin, reabsorption, and concentration of urine [39]. The role of the kidney as the primary eliminator of exogenous drugs and toxins, in addition to the fact that it is characterized by a large volume of blood supply which ensures a high level of toxicant delivery over a period of time, predisposes this important organ to nephrotoxicity and enhances its vulnerability to developing various forms of injury [40], [41]. The serum levels of urea, uric acid and creatinine are often used as markers for kidney function [42], [43]. The highly significant increase ($p < 0.05$) noticed in this study in the concentration of serum urea, uric acid, potassium ion and creatinine in the group administered 200 mg/kg and 400 mg/kg body weight doses is noteworthy. The increased level of these biomarkers is a pointer to the nephrotoxicity potential of the extract at 200 and 400 mg/kg dose levels. This result corroborates the work of References [44] and [45] who reported toxic diterpene and ingenane esters from known medicinal plants. Also, *Alstonia boonei*, one of the 10 most commonly used folkloric medicinal plants in southwest Nigeria as reported [46] in spite of the numerous benefits, has been shown to be capable of causing nephrotoxicity upon its chronic consumption [47], [48]. It can therefore be explained that possibility of toxicity could not be completely ruled out in a plant as a result of having some therapeutic properties which form the basis for safe dosage level.

The histopathological examination confirmed the different levels of damage suffered by the liver and kidneys of rats administered 200 mg/kg and 400 mg/kg dose levels of SDELE for a period of fourteen weeks. At the lower dose, there was a mild haemorrhage which proceeded to affect a large portion of the liver at 400 mg/kg body weight dose. Basically, when haemorrhage occurs on a robust tissue like the liver, the tissue responds in a reactive or a reparative process to form fibrosis with concomitant change in the morphology and function of such tissue. The histo-architecture of the kidney also revealed haemorrhage and vascular congestion at 200 mg/kg dose and renal damage at 400 mg/kg body weight dose respectively, confirming the toxicity of SDELE at these dose levels to the organ at chronic administration. However, the liver and kidney were not affected by the extract at 100 mg/kg body weight dose upon

chronic administration indicating the safety of the extract to these two organs at that concentration.

V. CONCLUSION

This research documents and scientifically elucidated the safety profiling of *Scoparia dulcis* ethanol leaf extract: a plant widely used as an anti-diabetic, immune stimulatory, aphrodisiac and blood cleansing/tonic agent. It is thus a good candidate for further research efforts as it shows tendencies of damaging the liver and the kidney on prolong usage. Herbal medicine is gaining more ground because of economic hardship especially in the third world countries and the belief of absence of side effects. However, this study which is first of its kind on *Scoparia dulcis* is an eye opener on the serious need to carry out comprehensive toxicity studies of all our medicinal herbs to strike a balance between cure and safety. Ethanol leaf extract of *Scoparia dulcis* has shown hepatotoxic and nephrotoxic tendencies at dose as low as 200 mg/kg body weight at chronic administration though it is very safe at 100 mg/kg body weight dose.

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