

Research Paper:

Toxicological Assessment of *Solanum Erianthum* Extracts in Albino Rats: Haematological, Biochemical and Histopathological Findings



Ngozi Maureen Uzoekwe¹ , Ikechukwu Peter Ejidike^{2*} , Mark Ehijele Ukhun³

1. Department of Physical Sciences, Faculty of Sciences, Benson Idahosa University, Okha, Benin City, Nigeria.

2. Department of Chemical Sciences, Faculty of Science and Science Education, Anchor University, Lagos, Nigeria.

3. Department of Chemistry, Faculty of Physical Sciences, University of Benin, Benin-City, Nigeria.



How to cite this paper Uzoekwe NM, Ejidike IP, Ehijele Ukhun M. Toxicological Assessment of *Solanum Erianthum* Extracts in Albino Rats: Haematological, Biochemical and Histopathological Findings. Iranian Journal of Toxicology. 2021; 15(1):37-48. <http://dx.doi.org/10.32598/ijt.15.1.728.1>

 <http://dx.doi.org/10.32598/ijt.15.1.728.1>



Article info:

Received: 16 Jul 2020

Accepted: 20 Sep 2020

Online Published: 01 Jan 2021

* Corresponding author:

Ikechukwu Peter Ejidike, PhD.

Address: Department of Chemical Sciences, Faculty of Science and Science Education, Anchor University, Ayobo, Lagos, Nigeria.

E-mail: iejidike@aui.edu.ng

ABSTRACT

Background: *Solanum erianthum* leaves extract has been used to treat sexually-transmitted diseases, malaria, and leprosy. This study assessed the toxicity and safety of *S. erianthum* extract in rats.

Methods: Treatment with 250, 500 or 750 mg/kg of the aqueous, ethanolic and methanolic extracts in the rats had different effects on the biochemical activities of the liver, heart and kidneys, and based on the hematological and histopathological changes observed after short-term (30 days) and long-term (60 days) exposure.

Results: The serum biochemical parameters examined were AST, ALT, and ALP concentrations in the albino rats treated with the extracts of *S. Erianthum* at various concentrations. The extract showed significantly different effects in the treated versus untreated rats ($P < 0.05$). The ALT level significantly decreased after the administration of 250, 500, or 750 mg/kg of the aqueous extract of *S. Erianthum*. There were significant differences in the hematological profile of the rats for all doses of the methanolic extracts ($P < 0.05$). Histopathological examinations detected Kupffer cells activation in the liver, otherwise normal histology of the kidneys with respect to the glomeruli and tubules. Also, mild coronary vascular congestion was detected in the animals' heart.

Conclusion: The *S. erianthum* extracts were safe and without exerting toxic effect on the rat's heart or kidneys, as demonstrated for the doses up to 750 mg/kg given over 30 or 60 days. However, the congestion in the rats' spleens could be a cause for concern if the extract were to be used in humans for long-term.

Keywords: *Solanum erianthum*, Hepatic macrophages, Serum chemistry, Toxicity, Sinus histiocytosis, Enzymatic activities

Introduction

The basis for the engineering of modern medicines revolves around medicinal plants, owing to the potentially useful chemicals found in them [1-3]. The plant kingdom symbolizes a vast reservoir of

bioactive constituents with several chemical arrangements, with both protective and disease-producing properties. Medicinal plants are the best sources of obtaining a variety of potential drugs as suggested by World Health Organization (WHO). In developing countries, about 80% of individuals use plant medicines, because of their historical experience with the beneficial com-

ponents i.e., phytochemicals, including terpenoids, steroids, flavonoids, alkaloids and tannins [1, 4, 5].

About 50% of drugs presently used in healthcare are originally of plant sources. However, not all plants with medicinal properties have been investigated and analysed methodically. To date, several reports have been published on the phytochemical properties of plants that possess evidence of health benefits [6, 7]. Nigeria is amongst the finest floristic region of the African continent and has been a rich source of medicinal plants since old ages. People have produced herbal material by diverse techniques to meet their needs, principally as foods or remedies [4, 7, 8].

Solanum erianthum (*S. erianthum*) is endemic to the northern areas of South America and southern parts of the United States (Figure 1). This plant has also been known in other parts of the world particularly across the tropical nations. Velvet nightshade, Potato tree, Mullein, nightshade (*S. donianum*), and Salvadoran are the common names. In West Africa, the leaf extracts from *Solanum* species are administered for the diuretic and laxative properties and the claimed benefits in the treatment of leprosy, malaria, communicable diseases, and liver disorders [9, 10]. *S. erianthum* is considered appropriate to make a hot drink; however, it is an undesirable plant in Ghana. It has been purposefully cultivated as a source for foods and remedy [11, 12].

Essential oils and extracts from the fruits and greeneries of *S. erianthum* have been investigated for their cytotoxicity alongside their traditional uses as medication, particularly for wound healing, skin diseases, and stomach-related illnesses [13, 14]. Decoction is a method of producing extracts by boiling herbal or plant material [15]. In India, decoctions of fruits are used for toothache, while raw fruits are applied specifically to avoid leech-bites among the communities in the Madurai District of Tamil Nadu [15].

In Oaxaca, Mexico, *S. erianthum* is known as an oral pain reliever for stomach aches and as an antimicrobial agent for skin wounds [16]. Like other species of its kind, *S. erianthum* has a number of ethnobotanical and pharmacological applications. Its properties may be attributed to the components, such as steroids, free genins, saponins, and steroidal alkaloids of the spiro-solane group, i.e., tomatidine and solasodine. Ndebia et al. [17] reported that the oral administration of *Solanum torvum* (Solanaceae) extract exhibited anti-inflammatory and analgesic effects. These properties justify the use of *Solanum* species in traditional and herbal medicine [17].

However, despite the widespread and traditional uses of this plant, comprehensive studies on its phytochemicals and health effects in humans and animals are scanty. Further, scientific evidence on its safety and toxicity is missing. This study, therefore, aimed at investigating the phytochemical potentials of *S. erianthum* leaves extract produced with three solvents: water, ethanol and methanol. The plant extract was administered to Albino rats at graded doses and the health effects were examined in the blood samples and essential organs, using hematological, biochemical and histopathological investigations.

Materials and Methods

Chemicals and equipment: All chemicals and reagents used in this study were of analytical grades and received from Sigma-Adrich (St Louis, USA). The chemicals were: Ethylene Diamine Tetra Acetic acid (EDTA) and biochemical enzyme kits to determine the serum levels of Alanine Phosphatase (ALP), Alanine Transaminase (ALT), and serum total proteins, which were performed colourimetrically.

Collection of plant material and extraction: Fresh mature leaves of *S. erianthum* were collected from the bushes in Benin City, Nigeria. They were identified and



Figure 1: The plant parts of *Solanum erianthum*.

validated by an expert plant botanist from the Department of Plant Biology and Biotechnology, University of Benin, Benin, Nigeria. The *S. erianthum* leaves were washed thoroughly, air-dried, and pulverized to a fine powder in a blender. About 6000g of the powder were extracted with 7.5 L of each of the solvents, followed by filtration and subsequent concentration in a rotary evaporator. This step was followed by freeze-drying to obtain a solid extract material.

Phytochemical tests: The phytochemical profiling of the extract was performed with few modifications based on the previously reported procedures [2, 4, 6-8, 12, 18-20].

Animal experiments: Albino rats weighing 120–140g were used for the purpose of this study. They were received from the disease-free stock of the Animal House, Department of Biological Sciences, University of Ibadan, Nigeria. They were housed in metal cages lined with wood shavings under standard environments of 12hr. light-dark cycle, temperature, relative humidity and adequate ventilation. The rats had free access to food and water ad libitum. The animals were allowed to acclimatize to the lab environment for one week, with the feed and water changed regularly and the cages cleaned daily.

Animal grouping and treatments: The rats were separated into five groups of 21 each. Groups 1 and 2 served as the controls, while Groups 3, 4 and 5 were administered orally with *S. erianthum* extract at doses of 250, 500 or 750 mg/kg, respectively. The assigned extracts were administered once daily by gavage and the animals were sacrificed at the end of 30 or 60 days, depending on the group assignment.

Collection and preparation of blood, serum and organs: At the end of the handling period per group, the rats were sacrificed, and the blood samples collected from the heart by cardiac puncture into EDTA-treated and lithium heparin tubes for hematological and biochemical tests. The collected organs were dissected out and immersed in formalin for later histological examinations. The lithium heparin tubes containing the sera were centrifuged for 10 minutes at 3000 rpm. The plasma was collected and used for the subsequent biochemical assays [3, 21, 22].

Biochemical assays: Serum Aspartate Transaminase (AST), Alanine Transaminase (ALT) and Alkaline Phosphatase (ALP) were estimated colorimetrically, using Randox reagent enzyme kits based on established methods [1, 23]. The absorbance values were converted to concentrations, using the Randox conversion table.

Calculations: The serum AST and ALT levels were extrapolated from a reference standard curve (provided with the Randox reagent kits), while ALP activity in IU/L was estimated by means of the following formula: $IU/L = (\text{Absorbance of sample} / \text{Absorbance of standard}) \times \text{Standard concentration}$.

Hematological assays: The hematological assays were evaluated with an auto-reader PC 210N Erma (Tokyo, Japan). The blood samples in the EDTA-treated tubes were used for full blood cell counts, including White Blood Cells (WBC), Hematocrit (HCT), Red Blood Cells (RBC), Hemoglobin (Hgb) and WBC differentials.

Histopathological & morphological studies: In order to evaluate the histological changes, the kidneys, heart, spleen and liver were fixed in formalin, sectioned and stained with haematoxylin and eosin. Detailed microscopic examinations of the organ sections were carried out for all animal groups. In each group, photomicrographs were obtained at two magnification levels of 100 and 400.

Statistical analyses: Following the statistical analyses, the data were expressed as the means \pm standard deviations (Mean \pm SD), and the differences among the groups (controls vs experimental) were evaluated by One-way Analysis of Variance (ANOVA), using Statistical Package for Social Sciences (SPSS) V. 18.

Results

Qualitative phytochemical screening: The results of the phytochemical profiling of the aqueous, ethanolic and methanolic leaf extracts of *S. erianthum* demonstrated that they possessed such properties for lowering blood sugar, and contained steroids, proteins, flavonoids, tannins, alkaloids, and saponins.

Biochemical effects of the extracts: Treatment with 250, 500 or 750 mg/kg of the aqueous, ethanolic and methanolic extracts showed varying effects on the biochemical activities of ALT, AST and ALP compared to the controls after short-term (30 days) and long-term (60 days) exposure. The results of these tests are presented in Tables 1-6.

Aqueous extract: As reflected in Table 1, the Alanine aminotransferase (ALT) levels significantly increased when 250 mg/kg of the aqueous extract was administered for 30 days. However, the 500 mg/kg dose had no significant effect. The serum AST level significantly increased compared to that of the controls at all concentrations of the aqueous extract. As shown in Table 2, the ALT levels significantly decreased with 250, 500 or 750

Table 1. Effect of aqueous extract on the biochemical parameters in albino rats (Day 30)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine aminotransferase (ALT)	3.96±0.07	4.76±0.40	4.44±0.52	3.94±0.06
Aspartate aminotransferase (AST)	6.96±0.14	38.85±0.79 ^a	7.20±0.35	15.73±0.43 ^a
Alkaline phosphatase (ALP)	169.76 ± 9.26	50.40±1.87 ^a	200.15±1.25 ^a	60.35±0.89 ^a

^aSignificantly different from that of the controls at P<0.05.**Table 2.** Effect of aqueous extract on the biochemical parameters in albino rats (Day 60)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine aminotransferase (ALT)	5.12±0.54	4.66±0.31	4.64±0.32	4.05±0.15
Aspartate aminotransferase (AST)	7.86±0.23	38.86±1.09 ^a	8.17±0.43	16.04±0.69 ^a
Alkaline phosphatase (ALP)	179.66±0.57	52.39±3.12 ^a	203.51±2.20 ^a	60.05±2.17 ^a

^aSignificantly different from that of the controls at P<0.05.**Table 3.** Effect of ethanolic extract on the biochemical parameters in albino rats (Day 30)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine Aminotransferase (ALT)	3.11±0.11	3.66±0.14	5.51±0.17 ^a	5.61±0.35
Aspartate Aminotransferase (AST)	12.74±0.23	54.22±0.69 ^a	63.59±0.42 ^a	13.81±0.17 ^a
Alkaline Phosphatase (ALP)	169.80±0.26	69.03±0.96 ^a	71.58±0.64 ^a	81.58±0.29 ^a

^aSignificantly different from that of the controls at P<0.05.**Table 4.** Effect of ethanolic extract on the biochemical parameters in albino rats (Day 60)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine aminotransferase (ALT)	3.31±0.20	4.27±0.47 ^a	5.61±0.09 ^a	4.92±0.86
Aspartate aminotransferase (AST)	13.72±0.25	54.45±1.07 ^a	53.03±1.46 ^a	52.87±1.42 ^a
Alkaline phosphatase (ALP)	170.30±1.54	69.03±0.96 ^a	71.69±0.77 ^a	71.60±1.12 ^a

^aSignificantly different from that of the controls at P<0.05.**Table 5.** Effect of methanolic extract on the biochemical parameters in albino rats (Day 30)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine aminotransferase (ALT)	3.05±0.05	62.43±0.37 ^a	13.28±0.25 ^a	22.16±0.17 ^a
Aspartate aminotransferase (AST)	2.30±0.34	12.42±0.12 ^a	10.41±0.11 ^a	9.22±0.19 ^a
Alkaline phosphatase (ALP)	169.63±0.55	119.41±0.35 ^a	253.41±0.37 ^a	157.27±0.26 ^a

^aSignificantly different from that of the controls at P<0.05.

Table 6. Effect of methanolic extract on the biochemical parameters in albino rats (Day 60)

Biochemical Parameter (IU/L)	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
Alanine aminotransferase (ALT)	3.97±0.04	63.67±2.08 ^a	55.17±0.04 ^a	22.19±0.74 ^a
Aspartate aminotransferase (AST)	2.78±0.11	5.60±0.44 ^a	9.35±0.05 ^a	7.52±0.25 ^a
Alkaline phosphatase (ALP)	172.63±0.55	120.12±0.13 ^a	144.54±0.47 ^a	150.38±0.33 ^a

^aSignificantly different from that of the controls at P<0.05.

Table 7. Hematological effects of *S. erianthum* aqueous extract in albino rats (Day 30)

Parameter	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
WBC (103/μL)	8.20±0.13	11.26±0.08 ^a	12.79±0.02 ^a	30.85±0.36 ^a
Lymphocyte (%)	5.66±0.08	5.45±0.06 ^a	9.35±0.07 ^a	8.70±0.14 ^a
Monocyte (%)	1.15±0.49	1.33±0.01	1.78±0.04	4.40±0.01 ^a
HGB (g/dl)	15.26±0.36	12.63±0.04 ^a	12.73±0.11	14.28±0.04
Hematocrit (%)	38.80±0.14	39.48±0.11 ^a	35.90±0.14	40.38±0.25 ^a
Platelet (103/μL)	915.50±0.71	843.30±0.42 ^a	678.00±1.41 ^a	872.50±0.71 ^a
RBC (Ml/mm ³)	6.65±0.21	5.84±0.01	6.27±0.04	6.65±0.01

^aSignificantly different from that of the controls at P<0.05;

WBC: White Blood Cells; HGB: Haemoglobin; RBC: Red Blood Cells.

Table 8. Haematological effects of *S. erianthum* ethanolic extract in albino rats (Day 30)

Parameters	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
WBC (103/μL)	12.40±0.01	7.25±0.03 ^a	9.60±0.14 ^a	8.64±0.05
Lymphocyte (%)	7.40±0.14	4.40±0.14	5.35±0.02 ^a	6.35±0.13 ^a
Monocyte (%)	6.67±0.15	6.87±0.11	6.30±0.35 ^a	6.52±0.64
HGB (g/dl)	14.35±0.21	16.30±0.28 ^a	14.22±0.16	13.35±0.21
Platelet (103/μL)	647.50±0.71	415.50±2.12	602.25±0.35 ^a	753.50±0.51
Haematocrit (%)	39.65±0.49	44.95±0.21 ^a	38.90±0.14 ^a	38.45±0.01 ^a
RBC (Ml/mm ³)	1.62±0.04	0.95±0.07 ^a	11.64±0.19	1.45±0.07

^aSignificantly different from that of the controls at P<0.05;

WBC: White Blood Cells; HGB: Haemoglobin; RBC: Red Blood Cells.

mg/kg of the aqueous extract of *S. erianthum* over 60 days. For 250 mg/kg, there was a considerable increase in AST but for 500 and 750 mg/kg, the increase was not as high as that of the 250 mg/kg. On the other hand, the ALP levels significantly decreased with 250 and 750 mg/kg doses compared to the untreated group (P<0.05).

Ethanolic extract: As shown in Table 3, the ALT levels significantly altered after treatment with 250, 500 or

750 mg/kg of the ethanolic extract. At 750 mg/kg dose, there was an increase in AST (30 days) but for 500 and 250 mg/kg the increase was much higher than that of the 750 mg/kg dose. Also, the ALP levels significantly changed at 250, 500 or 750 mg/kg doses compared to of the untreated groups. For the long-term effects (60 days), the ALT levels significantly increased at 250, 500 or 750 mg/kg doses of the ethanolic extract (Table 4). At 250

Table 9. Haematological effects of *S. erianthum* methanolic extract in albino rats (Day 30)

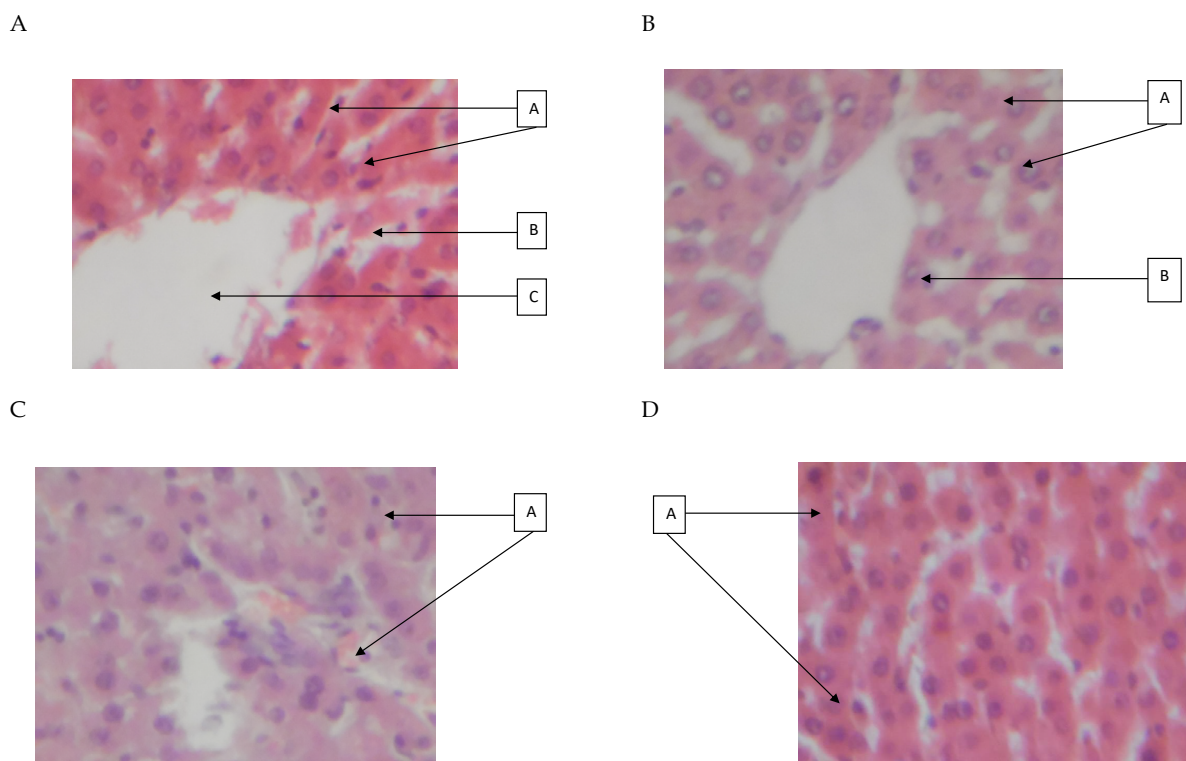
Parameters	Mean±SD			
	Control (Undosed)	250 mg/kg	Dosages 500 mg/kg	750 mg/kg
WBC (103/ μ L)	12.37±0.05	14.95±0.12 ^a	6.60±0.14 ^a	10.95±0.08 ^a
Lymphocyte (%)	7.35±0.03	10.70±0.14 ^a	3.93±0.04 ^a	6.95±0.64
Monocyte (%)	1.63±0.04	1.64±0.06	0.76±0.08 ^a	1.19±0.02
HGB (g/dl)	14.30±0.42	15.60±0.11 ^a	12.40±0.57 ^a	11.78±0.04 ^a
Haematocrit (%)	32.75±1.06	43.90±0.13 ^a	37.05±0.78 ^a	34.15±0.49 ^a
Platelet (103/ μ L)	845.50±3.54	694.00±7.07 ^a	759.50±3.54 ^a	603.25±0.35 ^a
RBC (Ml/mm ³)	6.86±0.01	6.74±0.02	5.60±0.28	6.10±0.03

^aSignificantly different from that of the controls at $P < 0.05$;

WBC: White Blood Cells; HGB: Haemoglobin; RBC: Red Blood Cells.

and 500 mg/kg doses, there were significant increases in the serum AST levels, but for 750 mg/kg the increase was not as high. However, the ALP levels significantly decreased for all of the doses (250, 500 & 750 mg/kg) compared to those for the untreated rats.

Methanolic extract: The ALT levels rose significantly with 250, 500 or 750 mg/kg of the methanolic extract after 30 days exposure compared to those for the untreated rats (Table 5). Also, the AST levels significant increased for all of the doses administered. The ALP levels on the other hand, changed meaningfully in response to the treatment

**Figure 2.** The liver photomicrographs

A: Microscopic section of normal rat liver (control) showing; A: Hepatocytes; B: sinusoids; and C: central vein;

B: Rat liver treated with 250 mg/kg aqueous extract showing; A: Normal hepatocytes; and B: Mild Kupffer cell activation;

C: Rat liver treated with 500 mg/kg methanol extract showing; A: Moderate Kupffer cell activation;

D: Rat liver treated with 750 mg/kg ethanol extract showing; A: Normal hepatocytes.

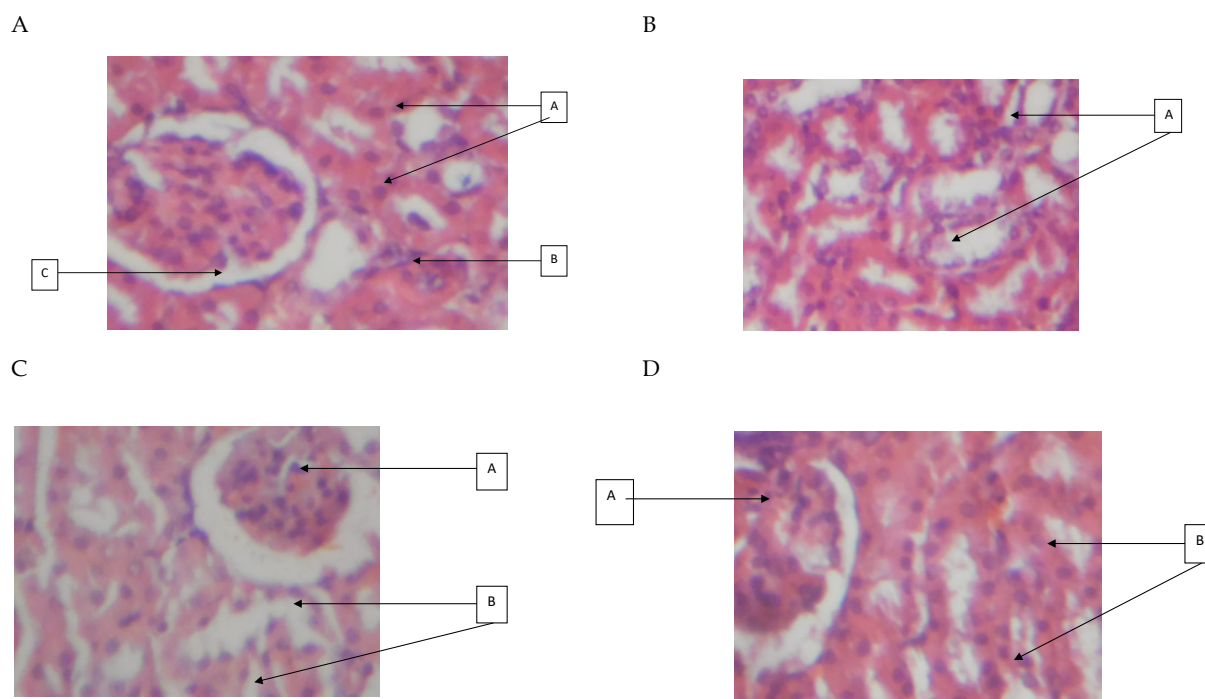


Figure 3. The kidney photomicrograph

A: Kidney section of normal control rat, showing: A: Tubules; B: Interstitial space; and C: Glomerulus;

B: Rat kidney treated with 250mg/kg aqueous extract showing: A: Normal tubules;

C: Rat kidney treated with 750mg/kg methanol extract showing A: Normal glomerulus; B: Tubules;

D: Rat kidney treated with 500mg/kg ethanol extract showing A: Normal glomerulus; B: Tubules.

with 250, 500 or 750 mg/kg doses as compared to those found for the untreated groups. For the long-term effect (60 days), the ALT levels significantly increased (Table 6) in response to 250, 500 or 750 mg/kg of the methanolic extract. Also, there were significant increases in AST at all doses of the extract. Conversely, the serum ALP levels significantly changed in response to the treatment at 250 or 750 mg/kg dosages compared to those noted for the untreated groups. Lastly, the AST, ALP and ALT levels differed significantly in rats treated with the extract for 30 or 60 days compared to the untreated rats at all concentrations used ($P < 0.05$).

Hematological findings: As shown in Tables 7, 8 and 9, there was an increase in white blood cells concentration following the aqueous extract administration. However, the use of the ethanolic and methanolic extracts led to decreases in WBC values as compared to those of the controls. Altered platelet concentration was also found for all doses of the extract administered to the rats (Tables 7, 8 & 9).

There was a significant difference within the hematological profile (WBC, RBC, Hgb, platelets, HCT, lymphocytes and monocytes) of the rats for all doses of the

methanolic extracts ($P < 0.05$). However, the values obtained were within a normal range. The results showed no deleterious effects of the extract on the blood cell counts and hemoglobin content.

Morphological and histopathological findings: The histological analyses showed cell structural changes in normal controls and those treated with the aqueous, ethanolic and methanolic extracts. After treatment of the groups with 250, 500 or 750 mg/kg doses of the extract, the liver, kidneys, heart, and the spleen showed evidence of structural alterations and injuries. The liver photomicrographs from the control group showed normal hepatocytes, sinusoids and the central vein (Figure 2A). The rat livers treated with 250, 500 or 750 mg/kg of the aqueous, methanolic, or ethanolic extracts showed mild to moderate kupffer cell activation (Figures 2B & D). The kidney photomicrographs from the control and all of the treated groups showed normal tubules, interstitial spaces and glomerular structures (Figures 3A & D).

The photomicrographs of the control hearts showed normal bundles of myocardial fibres, coronary arteries and

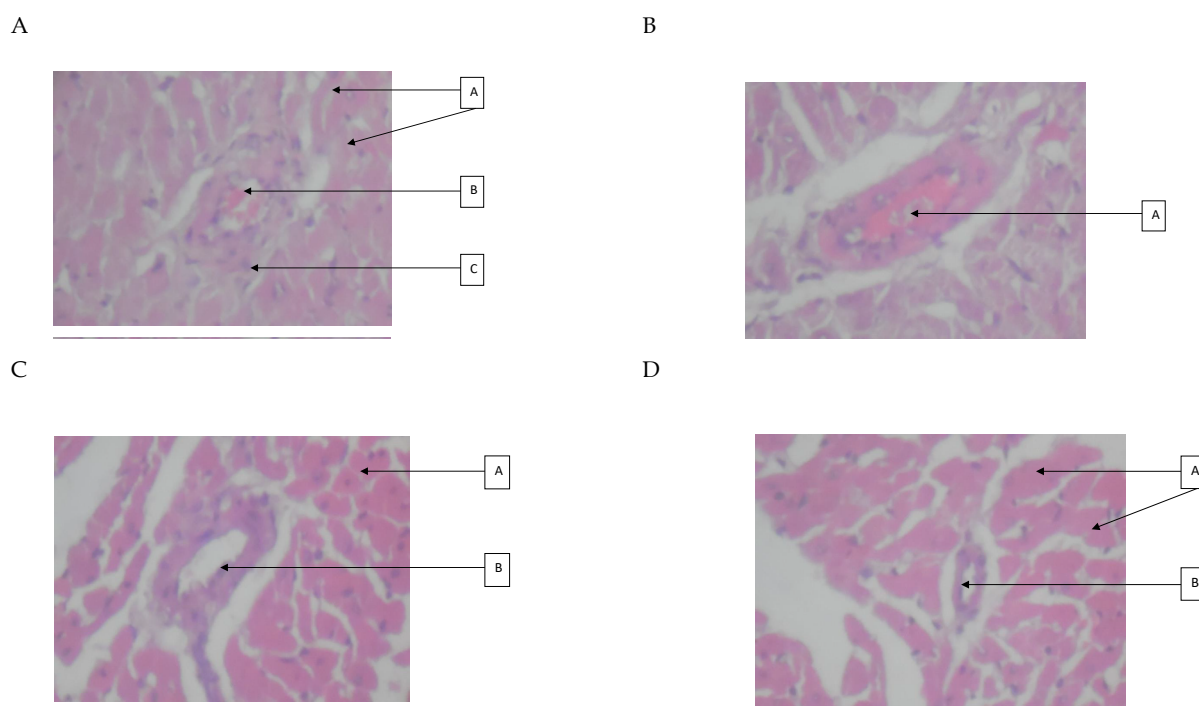


Figure 4. The photomicrographs of the control hearts

A: Heart section of normal control rat showing A: Bundles of myocardial fibres; B: Coronary artery; and C: Interstitial space;

B: Rat heart treated with 250 mg/kg aqueous extract showing A: Mild coronary vascular congestion;

C: Rat heart treated with 250 mg/kg methanol extract showing A: Normal myocardial fibres; B: Coronary artery;

D: Rat heart treated with 750 mg/kg ethanol extract showing A: Normal myocardial fibres; B: Normal coronary artery.

interstitial spaces (Figure 4A). However, the treatment with 250, 500 or 750 mg/kg of the aqueous, methanolic or ethanolic extracts revealed mild congestion in the coronary vasculature, but normal myocardial fibres and coronary arteries (Figures 4B & D). Whereas the control photomicrographs from the rats' spleens showed white and red pulps (Figure 5A). The treatment with 250-750 mg/kg of the aqueous, methanolic or ethanolic extracts revealed normal to mild follicular activation of the spleen with mild to moderate degrees of sinus histiocytosis and mild arteriolar dilation, and congestion (Figures 5B & D).

Discussion

Phytochemical findings: Phytochemicals are secondary plant metabolites, known to exhibit diverse pharmacological and biochemical effects on living organisms [2, 4, 18, 20, 21]. The qualitative analyses of phytochemicals remain the vital aspects of pharmacognosy [5, 8, 20]. Phytochemical screening of the *S. erianthum* extracts has led to the discovery of saponins, alkaloids, steroids, reducing sugar, flavonoids, protein and tannins. These phytochemicals exhibit various pharmacological and bio-

chemical effects when ingested by animals [1, 5, 6, 8, 18]. The qualitative phytochemical screening and findings of *S. erianthum* were in disagreement with those reported by Xavier et al. [12]. They did not detect alkaloids, glycosides, flavonoids and catechin in the extracts of this plant.

Hematological findings: The extracts of *S. erianthum* leaves reflected a surprising trend. There was an increase in white blood cell counts following the administration of the aqueous extract. However, the administration of ethanolic and methanolic extracts led to decreases in WBC values as compared to that of the controls. This may be due to complex chemical reactions. The altered platelet count was also found for the ethanolic and methanolic extracts administered to the rats. This may explain why *S. erianthum* is usually used in the treatment of skin diseases since platelets are involved in clotting and lead to the subsequent wound healing. Some of the enzymes find their way into the serum, probably by leakage during tissue damages. Valuable tools in the clinical diagnosis that provide evidence on the consequence of pathological damages to any tissue are linked to serum enzyme levels [3, 10, 21, 24]. An increase in the serum

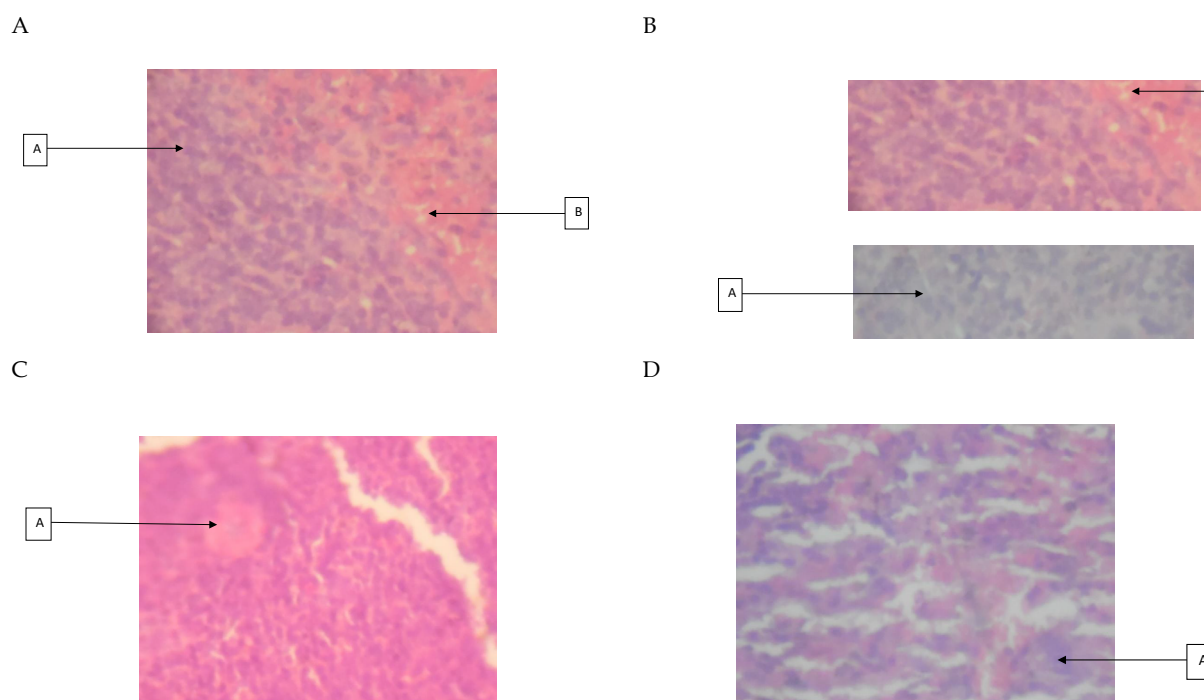


Figure 5. The control photomicrographs from the rats' spleen

A: Rat spleen section of normal control sample showing A: White pulp; and B: Red pulp;

B: Rat heart treated with 250 mg/kg aqueous extract showing A: Mild follicular activation; and B: Moderate sinus histiocytosis;

C: Rat spleen treated with 500 mg/kg methanol extract showing A: Normal follicular architecture;

D: Rat spleen treated with 250 mg/kg ethanol extract showing A: Mild sinus histiocytosis.

ALP may be the sign of hepatic impairment probably by the altered cell membrane, causing seepage of the enzymes into the serum [24, 25].

The analysis of the blood parameters is pertinent to risk assessment as alterations in the hematological system provide a higher prognostic value in human poisoning than those interpreted from animal experiments [3, 25]. Major alterations within the hematological parameters constitute WBC, RBC, Hgb, platelets, hematocrit, lymphocytes and monocytes levels. In this study, we observed mild changes within normal ranges for all doses of the methanolic extracts ($P < 0.05$). The results showed no deleterious effects on blood cell counts and hemoglobin concentration, thereby suggesting that the extract had no toxic effect on the blood [25]. This study revealed that the hematological parameters in rats treated with the various doses of the ethanolic extract were not outside the normal range. These findings were consistent with those reported by other studies, indicating the lack of significant consequences by the various plant extracts on the hematological parameters [21, 22, 26].

Biochemical findings: The increases in the concentrations of serum transaminase enzymes are suggestive of hepatic impairment in the rats [3]. Investigations of the liver function enable the assessment of the normal release of serum ALP, AST, and ALT. In liver pathologies, these enzymes leak into the blood depending on the extent of tissue damages [27, 28]. Aminotransferases constitute enzymes that catalyze the conversion of amino acids and α -keto acids via amino groups transfer. The enzymatic activities measurement of AST and ALT are of medical and toxicological significance, suggestive of liver damages by toxins [7, 28]. The AST levels increased in this study; however, ALT is a better marker of hepatocellular damage [29].

Upon examining the effects of the aqueous, ethanolic and methanolic extracts on the biochemical parameters, significant increases in serum AST and ALT levels were observed in response to 250, 500 or 750 mg/kg of the extract together with a marked decrease in the ALP level. The increases in AST and ALT levels may indicate impaired liver function caused by the most of the extract doses, as evident by the presence of mild kupffer cells

activation (Figures 2B & C). These observations agree with the previous reports, noting that ALP elevation denotes disturbed liver excretory functions. Severe liver injury is reflected by the elevations in the mitochondrial enzymes and serum AST and ALT [25, 28].

AST is usually assessed clinically to screen for liver normal function. Nevertheless, it should be noted that the origin of AST, and to a lesser extent ALT in the blood, may suggest the presence of abnormal conditions the liver and organs. Indeed, if the AST level is higher than the ALT, a more detailed investigation of the liver enzymes should be attempted. For instance, muscle inflammatory conditions as a result of dermatomyositis may cause AST to rise more than that of ALT while choline deficiency may cause serum ALT to rise. It has been confirmed that ALT and AST levels are not good indicators of liver functions on their own, since they do not reliably replicate the synthetic capability of the liver [27-29]. Such an elevation was observed in this study as a result of the administration of 250, 500 or 750 mg/kg of the *S. erianthum* extract, which could be due to choline deficiency [30]. On the other hand, the ALP levels were significantly lower after the administration of 250 or 750 mg/kg doses compared to those for the normal controls. This might be due to cellular membrane damages, since ALP is a membrane bound enzyme. Again, it could be as a result of malnutrition, e.g. celiac disease or deficiency in certain vitamins and minerals [30].

Histological effects: Histopathological examination of liver, kidneys, spleen and heart tissues did not reveal any acute or chronic condition resulting from the effect of the aqueous, methanolic and ethanolic extracts. However, there was a mild activation of Kupffer cells noted. Kupffer cells are hepatic macrophages that reside in the lumen of the liver sinuses [31]. They are activated subsequent to liver injuries and hepatocellular necrosis, leading to the release of inflammatory mediators [31].

Liver plays a major role in the body metabolism and participate in the decomposition of red blood cells, glycogen storage, hormone production, synthesis of plasma protein, excretion of waste materials, xenobiotic metabolism, and most drugs [22, 25]. The histopathologic results of the kidneys revealed normal tubules, interstitial space and glomeruli, and did not show signs of glomeronephritis, suggesting the safety of the extract.

The histopathological results from the rats' heart tissue samples following the administration of the graded doses of the aqueous, methanolic and ethanolic extracts revealed mild vascular congestion in both the heart and spleen.

Normal bundle of myocardial fibres and coronary arteries were observed, indicative of the mild inflammatory effect of the extract on the heart and the coronary vasculature.

In the rats' spleen tissue, the aqueous extracts induced a significant activation of the sinus histiocytosis with the administered 250 mg/kg. However, normal follicular architecture was observed in the spleen with 500 or 750 mg/kg of the aqueous extract. Moreover, treatment with graded doses of methanolic or ethanolic extracts caused mild follicular activations. Again, these findings signify that the extract's activation of the immune system in the spleen at low doses. Lastly, there was no indication of toxic damage by the extract in the heart and spleen tissues.

Conclusions

This paper investigated the phytochemicals in the aqueous, ethanolic and methanolic extracts of *S. erianthum* leaves. Based on the results, we can conclude that the phytochemicals are of clinical importance due to their nutritional constituents and their hematological, biochemical and histological effects as shown in albino rats. These properties may be extrapolated to health benefits in humans. However, significant rises in the serum AST and ALT in rats in response to doses of the extract calls for exercising caution if used in humans. The isolation and molecular identification of the extract's bioactive constituents await future research on the extract.

Ethical Considerations

Compliance with ethical guidelines

The guidelines governing the use laboratory animals as described by the Committee on Ethics for Medical and Scientific Research, the University of Ibadan, Nigeria, was fully observed by the authors. Also, the internationally accepted standards for the use and care of laboratory animals, as described in the Canadian Council on Animal Care Guidelines and Protocol Review were equally practiced.

Funding

Benson Idahosa University financially supported this study.

Author's contributions

Conceptualization: Ngozi Maureen Uzoekwe. Mark Ehijele Ukhun; Methodology, writing – review & editing investigation, resources: All authors; Writing – Original Draft: Ikechukwu Peter Ejidike; Supervision: Mark Ehijele Ukhun.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgements

The authors are thankful to Benson Idahosa University, Okha, Benin City, Nigeria for Funding Subsidy.

References

- [1] Uzoekwe NM, Hamilton-Amachree A. Phytochemicals and nutritional characteristics of ethanol extract of the leaf and bark of Njangsa (*Riciodendron Heudelotii*) plant. *J Appl Sci Environ Manage.* 2016; 20(3):522-7. [DOI:10.4314/jasem.v20i3.5]
- [2] Mtunzi FM, Ejidike IP, Ledwaba I, Ahmed A, Pakade VE, Klink MJ, et al. Solvent-solvent fractionations of *Combretum erythrophyllum* (Burch.) leave extract: Studies of their antibacterial, antifungal, antioxidant and cytotoxicity potentials. *Asian Pac J Trop Med.* 2017; 10(7):670-9. [DOI:10.1016/j.apjtm.2017.07.007] [PMID]
- [3] Alawode AR, Dauda M, Adegbola AG, Babatunde OR. Biochemical and hematological effect of *Cordyla pinnata* following acute and sub-acute exposure to *Rattus norvegicus*. *Iran J Toxicol.* 2020; 14(1):43-50. [DOI: 10.32598/IJT.14.1.43]
- [4] Mtunzi FM, Ejidike IP, Matamela T, Dikio E, Klink MJ. Phytochemical profiling, antioxidant and antibacterial activities of leaf extracts from *Rhus leptodictya*. *Int J Pharmaco Phytochem Res.* 2017; 9(8):1090-9. [DOI:10.25258/phyto.v9i08.9616]
- [5] Motsumi PT, Qwebani-Ogunleye T, Ejidike IP, Mtunzi FM, Nate Z. *Teedia lucida* root extracts by ultrasonication and maceration techniques: Phytochemical screening, antimicrobial and antioxidant activity. *Rasayan J Chem.* 2020; 13(1):423-33. [DOI:10.31788/RJC.2020.1315594]
- [6] Khumalo B, Qwebani-Ogunleye T, Ejidike IP, Mtunzi FM, Pinkoane M. Evaluation of immune booster formulation by traditional health practitioners: antioxidants and mineral elements studies. *IntJ Pharma Bio Sci.* 2018; 9(2):29-37. [DOI:10.22376/ijpbs.2018.9.2.p29-37]
- [7] Singh CR. In vitro conservation, phytochemical analysis and antimicrobial effect of leaf and leaf derived callus extract of medicinally important *Cleome felina* L. *Acad J Med Plants.* 2020; 8(4):048-055. [DOI:10.15413/ajmp.2020.0107]
- [8] Chikezie PC, Ibegbulem CO, Mbagwu FN. Bioactive principles from medicinal plants. *Res J Phytochem.* 2015; 9(3):88-115. [DOI:10.3923/rjphyto.2015.88.115]
- [9] Sodipo OA, Abdulrahman FI, Sandabe UK, Wampana B. Comparative assessment of the total lipid profile, faecal cholesterol, very low density lipoprotein cholesterol (VLDL-C) and atherogenic index (A.I.) of the aqueous fruit extract of *Solanum macrocarpum*, α -solanidine and anti-hyperlipidaemic drugs on triton-induced hyperlipidaemic rats. *Greener J Med Sci.* 2013; 3(1):008-017. [DOI:10.15580/GJMS.2013.1.120212312]
- [10] Babaola O, Agbi J, Badiora A, Areola O. Protective effects of *Solanum erianthum* D. Don leaf extract on lead-induced toxicity in Wistar rats. *J App Pharm Sci.* 2016; 6(10):113-23. [DOI:10.7324/JAPS.2016.601016]
- [11] Kaunda JS, Zhang Y. The Genus *Solanum*: An ethnopharmacological, phytochemical and biological properties review. *Nat Prod Bioprospect.* 2019; 9:77-137. [DOI:10.1007/s13659-019-0201-6]
- [12] Xavier TF, Auxilia A, Senthamil SM. Antibacterial and phytochemical screening of *Solanum erianthum* (D. Don.). *J Nat Prod Plant Resour.* 2013; 3(2):131-3. <https://www.scholarsresearchlibrary.com/articles/antibacterial-and-phytochemical-screening-of-solanum-erianthum-d-don.pdf>
- [13] Essien EE, Ogunwande IA, Setzer WN, Ekundayo O. Chemical composition, antimicrobial, and cytotoxicity studies on *S. erianthum* and *S. macranthum* essential oils. *Pharm Biol.* 2012; 50(6):474-80. [DOI:10.3109/13880209.2011.614623] [PMID]
- [14] Bhargavi CS, Swamy V, Bilal S, Ushasri S, Ranjith Kumar J. Wound healing activity of alcohol extract of *Solanum erianthum* D. Don in excision and incision method. *Int J Res Ayurveda Pharm.* 2013; 4(1):109-13. [DOI:10.7897/2277-4343.04143]
- [15] Vimalanathan S, Ignacimuthu S, Hudson JB. Medicinal plants of Tamil Nadu (Southern India) are a rich source of antiviral activities. *Pharm Biol.* 2009; 47(5):422-9. [DOI:10.1080/13880200902800196]
- [16] Villa-Ruano N, Zurita-Vásquez GG, Pacheco-Hernández Y, Betancourt-Jiménez MG, Cruz-Durán R, Duque-Bautista H. Anti-lipase and antioxidant properties of 30 medicinal plants used in Oaxaca, México. *Biol Res.* 2013; 46(2):153-60. [DOI:10.4067/S0716-97602013000200006] [PMID]
- [17] Alawode TT, Lajide L, Owolabi, BJ, Olalaye MT, Ilesanmi OB. Phytochemical investigation, in vitro antioxidant and anti-inflammatory evaluation of leaf extracts of *Solanum erianthum*. *Curr J Appl Sci Technol.* 2017; 24(5):1-11. [DOI:10.9734/CJAST/2017/37389]
- [18] Ndebia EJ, Kamgang R, Nkeli-Chungag BN. Analgesic and anti-inflammatory properties of aqueous extract from leaves of *Solanum Torvum* (Solanaceae). *Afr J Tradit Complement Altern Med.* 2006; 4(2):240-4. [DOI:10.4314/ajtcam.v4i2.31214] [PMID] [PMCID]
- [19] Valluri LE, Krishna KSM, Madhu CH. Phytochemical screening and in vitro antioxidant potential of hydroalcoholic extract from the aerial parts of *Bryonopsis laciniosa*. *Int J Pharm Bio Sci.* 2017; 8(4):109-18. [DOI:10.22376/ijpbs.2017.8.4.p109-118]
- [20] Makanyane DM, Ejidike IP, Ssemakalu CS, Mtunzi FM, Pakade VE, Klink MJ, et al. GC-MS analysis and extraction optimization of bioactive compounds from *Pelargonium graveolens* L'Hér methanolic extract and their activities as pharmacological agents. *Int Res J Pharm.* 2019; 10(9):59-72. [DOI:10.7897/2230-8407.1009263]
- [21] Amos TN, Bashir L, Saba SE, Saba MA, Mohammed BM, Abdulsalam IH, et al. Phytochemicals and acute toxicity profile of aqueous and methanolic extracts of *Crateva adansonii* leaves in Swiss albino rats. *Asian J Biochem.* 2015; 10(4):173-9. [DOI:10.3923/ajb.2015.173.179]

- [22] Ojo OO, Ajayi SB, Nwaechefu OO, Ejidike IP. GC-MS analysis and attenuation of bleomycin-induced lung fibrosis by fractionated methanolic extract of *Cissampelos Owariensis* in Wistar rats. *J Herbs Spices Med Plants*. 2020; 26(2):155-71. [DOI:10.1080/10496475.2019.1689541]
- [23] Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. *Am J Clin Pathol*. 1957; 28(1):56-63. [DOI:10.1093/ajcp/28.1.56] [PMID]
- [24] Appidi JR, Yakubu MT, Grierson DS, Afolayan AJ. Toxicological evaluation of aqueous extracts of *Hermannia incana* Cav. leaves in male Wistar rats. *Afr J Biotechnol*. 2009; 8(10):2016-2020. [DOI:10.5897/AJB08.1067]
- [25] Ramanathan N, Tan E, Loh LJ, Soh BS, Yap WN. Tocotrienol is a cardioprotective agent against ageing-associated cardiovascular disease and its associated morbidities. *Nutr Metab (Lond)*. 2018; 15:6. [DOI:10.1186/s12986-018-0244-4] [PMID] [PMCID]
- [26] Contreras AU, Mebratu Y, Delgado M, Montano G, Hu CAA, Rytter SW, et al. Deacetylation of p53 induces Autophagy by suppressing Bmf expression. *J Cell Biol*. 2013; 201(3):427-37. [DOI:10.1083/jcb.201205064] [PMID] [PMCID]
- [27] Owoyele BV, Oyelowo OT, Biliaminu SA, Alaran ON, Alimi SA, Saliu RS. Haematological and biochemical studies on *Parquetina nigrescens* root extract in albino rats. *J Appl Pharm Sci*. 2011; 1(10):176-9. https://www.japsonline.com/admin/php/uploads/323_pdf.pdf
- [28] Yusuf AA, Lawal B, Yusuf MA, Omonije EO, Adejoke AO, Raji FH, et al. Free radical scavenging, antimicrobial activities and effect of sub-acute exposure to Nigerian *Xylopiya aethiopia* seed extract on liver and kidneys functional indices of albino rat. *Iran J Toxicol*. 2018; 12(3):51-8. <http://ijt.arakmu.ac.ir/article-1-668-en.html>
- [29] Saleem MTS, Chinni KV, Soumya G, Burra S, Hafeez S, Babu R, et al. Pre-clinical toxicological evaluation of *Rostelularia diffusa*: Hematological, biochemical, and histopathological studies. *PTB Rep*. 2017; 3(3):66-9. [DOI: 10.5530/PTB.2017.3.13]
- [30] Amtul Z, Uhrig M, Wang L, Rozmahel RF, Beyreuther K. Corrigendum to "Detrimental effects of arachidonic acid and its metabolites in cellular and mouse models of Alzheimer's disease: structural insight". *Neurobiol Aging*. 2012; 33(4):831.e21-831.e31. [DOI:10.1016/j.neurobiolaging.2017.12.007] [PMID]
- [31] Adeleye GS, Nneli R, Nwozor CM, Emesiana MC. Effects of coartem and artesunate on some haematological and biochemical parameters in albino rats. *Afr J Biomed Res*. 2012; 15(2):55-8. <https://www.semanticscholar.org/paper/Effects-of-Coartem-and-Artesunate-on-Some-and-in-Adeleye-Nneli/2973e6f21bdddf70eef27204ca3f810b1481351a>