# EFFECT OF NINETY-DAY REPEATED ADIMINISTRATION OF LEAF EXTRACT OF *Solanum anomalum* ON RATS


## Abstract

The leaves and fruits of *Solanum anomalum* Thonn. ex Schumach is used locally for the treatment of pains, fever and malaria among others. Effect of 90-day repeated administration of *S. anomalum* leaf extract on rats was investigated. Oral administration of the leaf extract (70, 140 and 210 mg/kg) to rats (male and female) was carried out daily for 90 days and the rats were sacrificed after being anaesthesized with light diethyl ether at the completion of the administration. Oral treatment of rats subchronically with *S. anomalum* leaf extract had no significant ($p>0.05$) effect on rats' body weights, hemoglobin concentration, WBC, RBC, platelets counts, percentages of PCV and eosinophils relative to control. However, percentages of neutrophils, monocytes and basophils were elevated significantly ($p>0.05$-$0.01$) at the highest dose (210 mg/kg), while lymphocytes percentage was reduced. The leaf extract had no significant ($p>0.05$) effect on bleeding and clotting time relative to control. The leaf extract non dose-dependently caused significant ($p<0.05$) lowering of ALT, AST and ALP levels. However, total and direct bilirubin levels were elevated significantly ($p<0.01$-$0.001$) only at raised leaf extract' doses (140 and 210 mg/kg). The leaf extract exerted no significant ($p>0.05$) changes on uric acid, bicarbonate, chloride, potassium and sodium levels, but lowered urea, creatinine, total cholesterol, triglyceride, HDL, VLDL and LDL levels of rats significantly ($p<0.05$) relative to control. There was no observable distortion of heart, testis and spleen histologies. Distortion in the histology of livers, kidneys, ovaries and brains of rats were observed at raised extract doses (140 and 210 mg/kg). High doses of the leaf extract should be avoided to prevent serious toxic effects.



**Keywords:** *Solanum anomalum*, subchronic, toxicity, organ weights

## Introduction

Medicinal plants are used world over in the treatment and management of diseases. Inspite of claims that these plants are natural and safe, there are reports of associated toxic effects which sometimes are taken for granted but may result in serious consequences such as organ damages, which can be attributed to toxic potentials of the main constituents [1]. Information on the toxic potentials of some these medicinal plants are inadequate or does not exist at all. This paucity of information needs to be address to enhance proper use of these plants.

*Solanum anomalum* Thonn. ex Schumach, are found in West and East Africa sub-regions growing and its parts are employed nutritionally and medicinally for the ttreatment of diabetes, gastrointestinal disorders, infections, inflammation and pains [1]. Hypoglycemic and antihyperglyaemic activities of the leaves have been reported[2]. Also, *in vivo* and *in vitro* antimalarial [3,4], anti-oedema [5], antioxidant and antiulcer [6], antiepileptic and depressant [7], antinociceptive [8], antidiarrhoeal [9], hepatoprotective[10,11], nephroprotective [12,13], genotoxic and cytotoxic [1] potentials of the leaf extract are reported in literature. The leaves are rich in tannins, alkaloids, flavonoids, saponins, diosgenin and diosgenin glycosides [2,3]. We report

in this study the effect of subchronic administration leaf extract of *Solanum anomalum* on rats.

## MATERIALS AND METHODS

### Plants collection

*Solanum anomalum* leaves were collected fresh in bush areas around Uruan area, Akwa Ibom State, Nigeria in August, 2020. Identification and authentication of the plant was carried out by a taxonomist in the Department of Botany and Ecological Studies, University of Uyo, Uyo, Nigeria and hebarium specimen (UUH.75a) was deposited at Department of Pharmacognosy and Natural Medicine Herbarium, University of Uyo.

### Extraction

The collected fresh leaves of *S. anomalum* were washed,chopped to smaller pieces and shade-dried for two weeks. The dried leaves were powdered using electric grinder. The powder (1.5 kg) was soaked in ethanol (50%) for three days at room temperature (28 ±2 ˚C), and thereafter filtered. The liquid filtrate was concentrated to dryness in *vacuo* 40˚C using a rotary evaporator (BuchiLab, Switzerland) and stored in a refrigerator at -4˚C, until used for the proposed experiments.

### Animals

Albino Wistar rats (138-150 g) of either sex were obtained from the University of Uyo animal house. They were maintained on standard animal pellets and water *ad libitum*. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics committee, University of Uyo.

**90-day toxicological study**

Adult wistar rats of both sexes were used in this study. They were weighed and randomly divided into four groups of 6 animals each and treated as follows; groups I, II, and III were respectively treated with *S. anomalum* leaf extract; 70, 140 and 210 mg/kg on alternate days for 90 days. Group IV was administered with distilled water (10 mL/kg) for the same period of time. At the end of the treatment period, the animals were weighed again and sacrificed under light ethyl ether vapour. Blood samples were collected by cardiac puncture and used immediately for haematological testing such as bleeding time, clotting time, full blood counts etc. Serum was separated from the remaining blood and stored at -20°C until used for biochemical determinations such as assay of liver and kidney functions as well as lipid profile etc.

The effect of the extract on some organs was studied. The organs; liver, kidney, spleen, brain, ovary, testis, and heart of rats were harvested and fixed in 10% formalin. The organs were processed, sectioned and stained using standard methods with hematoxylin and eosin (H&E).

**Haematological Analysis**

Haematological indices such as full blood count, total and differential White blood Cell Count (WBC), platelet count, haemoglobin concentration (Hb) and Packed Cell Volume (PCV) were estimated using automated Haematology analyser at Haematology Department of University of Uyo Teaching Hospital

**Biochemical determinations**

**Determination of the effect of the crude extract on the lipid profile indices of the treated rats**

The various lipid profile indices such as total cholesterol, triglyceride and high density lipoprotein (HDL) levels of the treated rats were determined enzymatically in serum using Randox diagnostic kits by colorimetric methods. Friedwald et al [14] formula was used to determined low and very low-density lipoprotein (LDL and VLDL).

**Effect of extract on Liver Function parameters**

Liver function parameters measured included liver enzymes (aspartate transaminase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP), total protein and albumin,total cholesterol, total and direct bilirubin. These were measured spectrophotometrically applying standard methods recommended by the

manufacturer [15] using Randox analytical kits at the Chemical Pathology Department of University of Uyo Teaching Hospital.

**Assay of Kidney function parameters**

The kidney function parameters determined were creatinine ,urea and electrolytes ( Na, K, Cl, and $HCO_3$ ) levels using diagnostic kits at the Chemical Pathology Department of University of Uyo Teaching Hospital;

**Histopathological Examination**

Buffered formalin was used to fix liver, kidney, spleen, brain, ovary, testis, and heart harvested from each rat that was used in this study. Standard methods of processing and staining with hematoxylin and eosin (H&E) were used at Department of Chemical Pathology, University of Uyo Teaching Hospital, Uyo to analyse the organs. Alterations in morphology were noted and recorded in each organ of sacrificed rat. Photomicrographs of the examined processed slides were taken.

**Statistical analysis**

Students' t-test and one –way analysis of variance followed by a post test (Tukey-Kramer multiple comparison test) were used to analyse data obtained from this study. Significant difference between means were considered at 5% ie $p \leq 0.05$.

## RESULTS

### Effect of leaf extract on Body weight

The effect of leaf extract on rats' body weight treated chronically with *S. anomalum* leaf extract for 90 days is shown in Table 1. The extract did not produce any significant ($p>0.05$) effect on the body weight of the treated rats' groups relative to control although the group treated with the middle dose of the extract (140 mg/kg) had the highest body weight gain.

### Effect on haematological parameters

Table 2 shows the effect of repeated administration of *S. anomalum* leaf extract on haematological indices of rats. Repeated treatment of rats with leaf extract of *Solanum anomalum* for 90 days did not affect the hemoglobin concentration, WBC, RBC and platelets counts prominently ($p>0.05$) relative to control. Similarly, PCV and eosinophils percentages were not affected by the treatment. However, percentages of neutrophils, monocytes and basophils were significantly ($p>0.05$-$0.01$) elevated in the rats' group treated with extract' highest dose (210 mg/kg) relative to control (Table 2). The extract treatment further caused significant ($p>0.05$) reduction in lymphocytes percentage in the group that received 210 mg/kg of the extract (Table 2). Moreso, treatment of rats for 90 days with *S. anomalum* leaf extract had

no effect on the bleeding and clotting time of treated rats relative to control (Figures 1 and 2).

**Effect of extract on liver function indices of rats**

There was a significant ($p<0.001$) non dose-dependent lowering of ALT and AST levels of rats following treatment with *S. anomalum* leaf extract (70-210 mg/kg) for 90 days relative to control (Table 3). Significant ($p<0.001$) lowering of ALP levels in groups treated with 70 and 210 mg/kg doses of the extract was also observed, while ALP level of rat group administered the extract (140 mg/kg) was observed to be significantly ($p<0.001$) elevated relative to control (Table 3). Leaf extracts' treatment further elevated direct and total bilirubin levels. These high levels were only significant ($p<0.05$-$0.001$) at extract doses of 140 and 210 mg/kg in the case of total bilirubin and significant ($p<0.01$) in groups treated with 70 and 140 mg/kg of the extract in the case of direct bilirubin, relative to control (Table 3).

**Effect on kidney function parameters of rats**

Treatment of rats for 90 days with leaf extract of *S. anomalum* produced a significant ($p<0.01$-$0.001$) non dose-dependent lowering of rats' creatinine levels relative to control (Table 4). Similarly, treated rats' urea levels were only lowered significantly ($p<0.05$) at 70 and 210 mg/kg doses of the extract relative to control (Table 4).

However, the levels of uric acid and electrolytes (bicarbonate, sodium, potassium and chloride) were unaffected by the extract treatment(Table 4).

**Effect of extract on lipid profile indices of rats**

Dose-dependent but insignificant ($p>0.05$) lowering of triglyceride, total cholesterol, LDL and VLDL levels were observed in rats following treatment with *Solanum anomalum* (70-210 mg/kg) leaf extract for 90 days relative to control. However, significant ($p<0.01$-$0.001$) dose-dependent lowering of HDL level was recorded following the same treatment relative to control (Table 5).

**Effect on histology of organs**

Figures 3 -11 show the effects of repeated treatment of rats with *S. anomalum* leaf extract for 90 days on histology of some organs. The leaf extract (70-210 mg/kg) did not produce any defect on the histology of the heart, testis and spleen (Figures 4, 8 and 9). The morphologies of these organs were normal as that of the control. Increased extract doses (140-210 mg/kg) were found to produce some defects such as mild defects observed as focal vacuolation in the purkinje layer and atrophied punkinje cells in the cerebella of the rats brains (Figure 3),distortion of liver parenchyma, array of hepatocytes and multiple focal area with inflammatory infiltrates in the liver parenchyma depicting portal and lobular inflammation (Figure

5), atrophied glomeruli, congested blood vessels in the cortex and interlobular haemorrhage in the kidney (Figure 6), and vacuolation in the langerhans islet of the pancreas (Figure 7), In the ovary, higher doses (140-210 mg/kg) caused hyperplasia of stromal interstitial cells which is associated with ovarian atrophy, atretic follicle with focal apoptotic cells. Few developing follicles were seen and demarcating connective tissue septa (Figure 10). On the uterus, higher doses (140 - 210 mg/kg), caused mild diffused eosinophilic inflammatory infiltration and increase in myometrium layer (Figure 11).

Table 1: Effect of repeated administration of *S. anomalum* leaf extract on body weights of rats

| Treatment<br><br>R&G /Extract | Dose<br><br>(mg/kg) | Initial body weight (Kg) | Final body weight (Kg) | Weight gain (Kg) |
|---|---|---|---|---|
| Control | 0.2ml | 148.2 · 3.78 | 236.0 · 2.82 | 87.8 · 2.69 |
| *S. anomalum* | 70 | 151.0 · 4.56 | 238.6 · 5.82 | 87.6 · 2.18 |
| | 140 | 155.0 · 2.87 | 249.0 · 4.52 | 94.0 · 2.63 |
| | 210 | 156.5 · 8.80 | 242.0 · 9.19 | 85.5 · 3.38 |

Data are expressed as mean ± SEM. Not significant relative to control $p>0.05$ .n = 6.

Table 2: Effect of subchronic administration of *Solanum anomalum* leaf extract on heamatological parameters of rats

| Treatment | Dose | WBC (L) | NEUT. (%) | LYM (%) | MONO (%) | ESINO (%) | BASO (%) | RBC (L) | HGB (g/dL) | PCV (%) | PLATELETS. (L) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10mg /ml | 12.61±0.50 | 21.40±1.30 | 75.76±1.86 | 1.83± 0.08 | 0.33± 0.05 | 0.35± 0.06 | 7.97± 0.30 | 13.70±0.46 | 44.08±1.20 | 847.5± 82.52 |
| Crude extract | 70 | 8.88±0.85 | 18.85± 1.79 | 76.71±2.61 | 2.76± 0.17 | 0.28 ±0.09 | 0.31± 0.07 | 8.13± 0.10 | 14.01±0.28 | 45.18±0.69 | 976.5± 68.85 |
| | 140 | 11.85±1.23 | 21.25±2.01 | 73.48±2.21 | 1.08± 0.09 | 0.35± 0.18 | 0.43± 0.05 | 8.27± 0.23 | 14.16±0.41 | 44.98±1.11 | 833.0± 47.49 |
| | 210 | 8.13±1.81 | 33.33 ± 2.60 [b] | 52.73±2.49[a] | 3.21±0.40[b] | 0.26± 0.11 | 0.78±0.09[b] | 7.41± 0.31 | 12.73±0.64 | 39.78±1.88 | 715.3± 85.68 |

Data are expressed as MEAN ± SEM, Significant at [a]$p<0.05$, [b]$p<0.01$, when compared to control. (n=6).

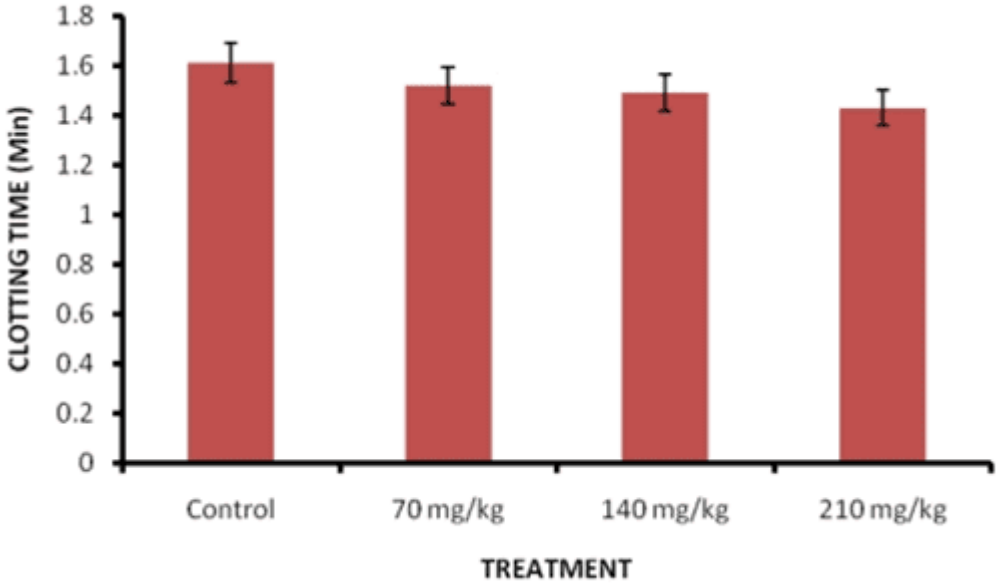


Figure 1: Effect of subchronic administration of *Solanum anomalum* leaf extract on clotting time of rats

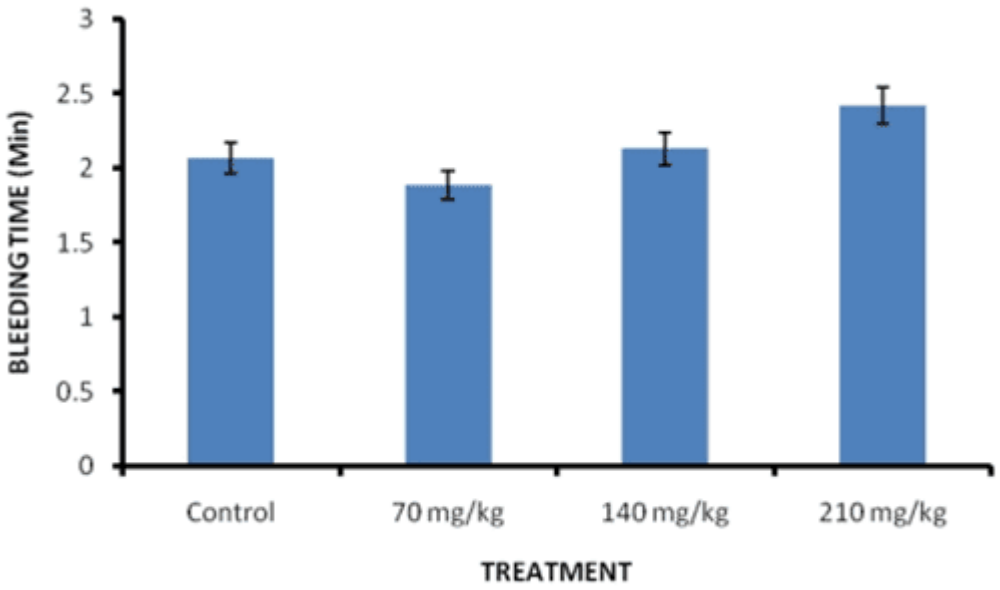


Figure 2: Effect of subchronic administration of *Solanum anomalum* leaf extract on bleeding times of rats

Table 3: Effect of subchronic administration of *Solanum anomalum* leaf extract on liver function parameters of rats

| TREATMENT | DOSE (mg/kg) | ALT (IU/L) | ALP (IU/L) | AST (IU/L) | Total Bilirubin (µmol/l) | Direct Bilirubin (µmol/l) |
|---|---|---|---|---|---|---|
| Control | 10 mg/ml | 139.83± 3.31 | 416.66±87.15 | 144.83±14.60 | 1.65±0.11 | 0.83±0.06 |
| Crude extract | 70 | 67.88±11.51[c] | 277.83±28.70[c] | 85.00± 6.15[c] | 2.05± 0.15 | 1.46±0.12[b] |
| | 140 | 58.66±14.09[c] | 512.66±66.74[c] | 75.00±4.05[c] | 2.21± 0.13[a] | 1.45±0.12[b] |
| | 210 | 66.83±14.99[c] | 255.02±18.90[c] | 86.16± 5.96[c] | 2.63± 0.13[b] | 1.13±0.13 |

Data are expressed as MEAN ± SEM, Significant at [a]p<0.05, [b]p< 0.01, [c]p< 0.001, relative to control. (n=6).

Table 4: Effect of subchronic administration of *Solanum anomalum* leaf extract on kidney function parameters of rats

| TREATMENT | DOSE (mg/kg) | CREATININE (mg/kg) | UREA (mg/dl) | URIC ACID (mg/dl) | BICARBONATE (mMol/L) | SODIUM (mMol/L) | POTASSIUM (mMol/L) | CHLORIDE (mMol/L) |
|---|---|---|---|---|---|---|---|---|
| Control normal saline | 10 mg/ml | 81.66± 2.53 | 9.21± 1.41 | 0.19±0.03 | 12.00± 0.81 | 146.3±1.33 | 6.00± 0.20 | 103.0± 0.00 |
| Crude extract | 70 | 58.33± 5.45$^{c}$ | 4.70± 0.72$^{a}$ | 0.16± 0.03 | 14.50± 1.11 | 147.6±3.18 | 5.76± 0.08 | 102.0± 1.20 |
| | 140 | 58.88± 4.74$^{c}$ | 5.33± 1.07 | 0.22± 0.02 | 10.16± 1.19 | 146.0± 0.57 | 5.50± 0.17 | 101.0± 1.52 |
| | 210 | 61.66± 6.10$^{b}$ | 4.36± 0.69$^{a}$ | 0.28± 0.05 | 12.16±1.32 | 144.0±1.00 | 6.06± 0.40 | 99.0± 1.52 |

Data are expressed as MEAN ± SEM, Significant at $^{a}p<0.05$, $^{b}p< 0.01$, $^{c}p< 0.001$, when compared to control. (n=6).

Table 5: Effect of subchronic administration of *Solanum anomalum* leaf extract on lipid profile of rats

| TREATMENT | DOSE mg/kg | TOTAL CHOLESTEROL (mMol/L) | TRIGLYCERIDE (mMol/L) | HDL-C (mMol/L) | LDL-C (mMol/L) | VLDL (mMol/L) |
|---|---|---|---|---|---|---|
| Control | 10 mL/kg | 1.70± 0.19 | 0.91± 0.17 | 0.63± 0.05 | 0.93± 0.11 | 0.35± 0.06 |
| Crude extract | 70 | 1.66± 0.10 | 0.78± 0.11 | 0.53± 0.02[b] | 0.75± 0.09 | 0.34± 0.05 |
| | 140 | 1.71± 0.10 | 0.73± 0.07 | 0.48± 0.04[c] | 0.77± 0.12 | 0.31± 0.03 |
| | 210 | 1.45± 0.16 | 0.63± 0.05 | 0.23± 0.04[c] | 0.81± 0.04 | 0.25± 0.02 |

Data are expressed as MEAN ± SEM, Significant at [b]p< 0.01, [c]p< 0.001, relative to control. (n=6).

## DISCUSSION

In this study, subchronic administration of the extract did not exert any considerable effect on the body weight of rats compared to untreated control, although there were insignificant weight gains with the different doses. Alterations of body weights serve as indicator of toxic effects of drugs or toxic agents which is considered serious in cases of significant loss of body weight [16]. In this study, moderately insignificant ($p>0.05$) improvement of rats body weights were observed in all the extract-treated groups relative to control group indicating that food intake and body growth processes of the rats were not affected negatively by the extract .

Determination of haematological indices is an important measure of intensity of toxic potentials of foreign compounds as well as plant extract on the blood [17], as this gives information on hemopoitic effect of these foreign compounds [18]. Subchronic treatment of rats with *Solanum anomalum* leaf extract for 90 days did not affect RBC, PCV, hemoglobin concentration, WBC, eosinophils and platelets counts significantly ($p>0.05$) relative to control. This might be an indication that there was no destruction of RBCs and/or inhibition of production of erythrocytes (erythropoiesis) [19] as well as leucocytosis. This also demonstrates that the extract has no erythropoeitin potential [20]. However, percentages of neutrophils, monocytes and basophils were significantly elevated at raised extract dose (210 mg/kg) relative to control. This suggest immunostimulatory effect of the extract to curb deleterious effect of the extract. The extract administration (at 210

mg/kg) further produced considerable lowering of lymphocytes percentage. Lymphocytes are important cells of the immune system [21]. The lowering of lymphocytes percentage observed in this study may suggest a depressive action on the immune system main cells. The inconsequential effect on the platelets suggest the adjustment of the animals to the extracts' effects.

In our study, exposure of rats to the leaf extract for 90 day lowered total protein and albumin levels significantly. The decreases observed in these serum proteins suggest liver damage resulting from compromised synthetic potentials of the hepatocytes. Albumin is needed in the body to maintain many physiologic functions in the body such as fluid pressure in the arteries and veins. Determination of serum albumin level gives information on the functionality of the liver as low level hepatic synthesis of albumin is indicative of end-stage liver disease or hepatic cirrhosis [22]. In this study, the extract caused significant decrease in serum albumin level. This observation corroborates the histopathological findings and is in agreement with previous finding that reduced serum/plasma albumin level correlates with hepatic damage [23]. In this study, significant lowering of serum total protein levels of rats that were treated with the leaf extract were recorded. lowered in serum total protein level reflects defective potentials of the hepatocytes to synthesize proteins [24,25] as was seen in this study. Evaluation of bilirubin (total and conjugated) level gives information on the excretory potentials of the liver [26]. Raised levels of direct and total bilirubin results from severe hemolysis [27]. Bilirubin, is an important liver function index [28]. The lowered total and direct bilirubin level as observed in this study with the leaf

extract suggest impairment of secretory function and an effect on the biliary system [29].

In this study, significantly reduced activities of AST, ALT and ALP were observed following subchronic treatment with *S. anomalum* leaf extract. Cellular enzymes often leak out of the cells when there is distortion of hepatocytes' architecture. Serum AST and ALT levels are used to determine acute and chronic hepatocellular damage [30]. Active form vitamin B6, pyridoxal-5-phosphate (PLP), serves as a coenzyme for both ALT and AST [31]. A number of factors such as metabolic, drugs and itrogenic activities as well as vitamin B6 deficiency could cause lowering of serum AST and ALT activities[32]. Deficiency of pyridoxal-5-phosphate has been found to correlate with lowered AST level in plasma and serum [33], which is also prominent in epileptic patients on anticonvulsant drugs [34]. The extract may have affected the liver and caused pyridoxal-5-phosphate deficiency. Alkaline phosphatase (ALP) is an important enzyme and indicator for the plasma membrane and endoplasmic reticulum [35]. The significant lowering of alkaline phosphatase activities after subchronic treatment of rats with leaves extract of *S. anomalum* can results from either leakage of membrane components (including ALP) into the extracellular fluid [36], deanaturation of the enzyme molecule *in situ* [37], or suspension of the enzyme activity at the cellular/molecular level. This can as well be due to gross lowering of concentration or complete absence of typical phospholipids needed for the proper functioning of the membrane bound enzyme [38].

Blood urea nitrogen (BUN) is a product of metabolic activities in the liver and is removed from the body in the urine through the kidney. It is found in high amount in the serum when there is kidney injury [39]. Breakdown of tissue creatinine gives rise to serum creatinine [39]. Therefore, high levels of urea and creatinine in the serum is indicative of kidney injury [40]. In this study, there were significant lowering of both serum creatinine and urea levels in rats administered with the leaf extract for 90 days. This indicates that the extract can affect the kidney adversely as seen in the histology of the kidney particularly at raised doses (140 and 210 mg/kg). The electrolytes concentrations were not affected by the extract treatment suggesting that the glomerular filtration rate was not affected by the treatment.

Abnormal changes in the concentration of lipid profile indices such as cholesterol, HDL, LDL and triglycerides serves as avenues to diagnose effect on the lipid metabolism as well as cardiac functions and diseases [41]. High blood cholesterol concentrations are an important risk factor for cardiovascular disease [42]. Therefore, the serum cholesterol lowering effect of the extract though insignificant may be clinically significant as the extract is unlikely to caused cardiovascular problem at the doses used. The lowered serum triacylglycerol level observed in this study may be a result of reduced lipolysis [41]. The lowering of VLDL, LDL and HDL levels in this study demonstrates a strong hypolipidemic potentials of the leaves perhaps due to inhibitory effect on lipolysis which is due to the activities of its phytoconstituents and may be an indication of the extracts' cardioprotective activity against lipid associated heart diseases [43].

On the histology, subchronic treatment of rats with *S. anomalum* leaf extract for 90 days did not produce any defect on the histology of the heart, testis and spleen, indicating that the extract has no deleterious effect on the heart, the male reproductive system and spleen. The morphologies of these organs were normal as that of the control. Raised extract doses (140-210 mg/kg) were found to produce some defects such as atrophied glomeruli, congested blood vessels in the cortex and interlobular haemorrhage in the kidney portraying a toxic effect on the kidney. These results are corroborated by the chemical pathology results which showed significant reductions in urea and creatinine levels. Furthermore, the leaf extract was found to cause distortion of liver parenchyma, array of hepatocytes and multiple focal area with inflammatory infiltrates in the liver parenchyma depicting portal and lobular inflammation, thus depicting hepatotoxic potential. These results corroborate the chemical pathology results which significant decreases in the levels of markers of liver functions were observed. In the ovary, higher doses (140-210 mg/kg) caused hyperplasia of stromal interstitial cells which is associated with ovarian atrophy, atretic follicle with focal apoptotic cells. Few developing follicles were seen and demarcating connective tissue septa. On the uterus, higher doses (140-210 mg/kg), caused mild diffused eosinophilic inflammatory infiltration and increase in myometrium layer. These findings depict adverse effect on the female reproductive system which also indicate contraceptive potentials. Also, the maximum dose (210 mg/kg) of the extract used in the study was found to produce mild defects observed as focal vacuolation in the purkinje layer and atrophied punkinje cells in the cerebella

of the rats brains, indicating adverse effects on the brain cells. Subchronic administration of the leaf extract to rats was also found to caused vacuolation in the langerhans islet of the pancreas portraying an adverse effect on the pancreas. However, no mortality was recorded throughout the period of chronic study.

## CONCLUSION

The findings of this study show that 90 days oral treatment of rats with *Solanum anomalum* leaf extract can cause mild to moderate toxic effects to the liver, kidney, brain, pancreas, ovary and uterus but has no effect on the hematological parameters except differential WBC elevation, testis, heart, spleen and lipid profile.

## AUTHORS' CONTRIBUTIONS

JEO,ICE - Research concept and design; JEO,ICE Animal studies, CCO,JAU Data analysis and interpretation; UUF,JAU,UPI Writing the article. JEO,JAU and UUF read and approved the final manuscript.

## COMPETING INTERESTS

The authors have not declared any conflict of interests.

## CONSENT

It is not applicable.

## EHTICAL APPROVAL

Approval for the study was given by Faculty of Pharmacy Animal Ethics Committee, University of Uyo.

## DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.


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