JSR Vol. 2(2), 2023: 75-87, ISSN: 2814-332

JOURNAL OF SCIENTIFIC RESEARCH
Department of Pure and Applied Chemistry
Faculty of Physical Sciences
University of Maiduguri
https://jsrunimaid.com

Research Article *https://doi.org/10.5281/zenodo. 10580548*

TOXICOLOGICAL PROFILE OF METHANOLIC EXTRACT OF *Sterculia setigera* FLOWERS ON BIOCHEMICAL PARAMETERS IN WISTAR RATS

Bitrus Chinda[1], Ibrahim Tijjani Babalola[1] and Abubakar El-Ishaq[2*]

[1]Department of Chemistry, Yobe State University, PMB 1144 Damaturu, Nigeria

[2]Department of Science Laboratory Technology, Federal Polytechnic PMB 1006 Damaturu, Nigeria

***Corresponding Author's Email Address**: *chemibrabal@yahoo.com, abubakaeelishaq.aei@gmail.com*

ABSTRACT

Sterculia setigera Del. is a plant used traditionally to treat different ailments. Presently, scanty information is available on the flower and its safety. The aim of this study is to determine the acute toxicity of the methanolic extract on vital organs and its associated biochemical indices. Fifteen female Wistar Albino rats were divided into five groups of three rats each. Group I served as control, group II, III, IV and V were orally administered daily of crude extract dissolved in distilled water at 5mg/kg BW, 50mg/kg BW, 300mg/kg BW and 1,000mg/kg BW. Rats were observed for 14 days and body weights were recorded. On day 15, the rats were sacrificed and blood samples were collected for biochemical and haematological analysis, while the livers and kidneys were sampled for histopathological examination. Body weight and haematology profile of treated rats showed significance difference ($p<0.05$) among means of HCT, MCV, MCHC, PLT and WBC. Histopathology result showed that kidneys appeared normal while livers showed mild periportal infiltration by inflammatory cells and focal mild microvesicular steatosis. However, hepatic enzymes were not significantly affected and no histopathological harmful effects were observed in kidney. In conclusion, methanolic extracts of S. setigera are safe up to 1,000mg/kg BW. The result obtained could be used to justify the folkloric usage of the plant for the treatment of different ailments.

Keywords: Pharmacological; Phytochemical; Medicine; Haematological; Herbal

INTRODUCTION

Several thousand people in Africa with partial access to systematized contemporary health support centres still depend on traditional systems of medicine to carter for their primary health care need [9]. *Sterculia setigera* belongs to the family Sterculiaceae and in Nigeria it has diverse common names; Hausa – "Kukkuki", Fulani – "bo'boli", Yoruba – "Ose-awere" [5]. It is a savannah tree in tropical Africa found in open savannah woodlands and seeds have a yellow aril [10]. Hamidu reported that it contains active secondary metabolites such as tannins, flavonoids, saponins, phenols and glycosides [11]. Research over the years has revealed that *S. setigera* possesses important pharmacological activities (Figure 1). These includes antioxidant, anti-tuberculosis, antimalarial, anti-inflammatory, and antidiarrheal, anti-spasmolytic [12,13,14,15,16,17,19].

There is an increased use of plant *Sterculia setigera* by various ethnic groups for different purposes across the globe [1], and is on the rise. The gum of this plant is used in the treatment of snake bites, leprosy, syphilis, coughs, bronchitis, rickets and to manage insanity [2]; [3].

Previous reports indicate that *S. setigera* is used in the treatment of jaundice [3]. Traditionally, the plant is also used as haematinics by traditional medical practitioners for postpartum women, people with symptoms of anemia, or those recuperating from one form of ailment or another [3]. Burnt mixture of the fruits and seeds are used to prepare black soap to cure dermatitis [4,5]. Bark of the plant decoction is used to treat diarrhea and dysentery in Nigeria [5,6,7]. The bark, shoots and seeds are used to prepared traditional medicines for the treatment of nasopharyngeal infections, pulmonary disorders, arthritis, rheumatism, syphilis, leprosy, dropsy, oedema, gout, boils whitlow, convulsion and epilepsy [8]. Its' flowers are used for the treatment of Jaundice, wound, leprosy and asthma [28,33,34].

In an *in vivo* toxicity study by [18]. *S. setigera* which extract administered at a maximum dose of 1000mg/kg per body weight of wistar albino rats was found to be nontoxic in two weeks study. Muhammad, Musa and Adamu, have reported that the stem bark extract of *S. setigera* is nontoxic which supported the continuous ethno-medicinal application of the plant as a curative agent of different diseases of clinical concern, with these, there is still scanty data regarding its toxicological effects on vital organs of the body [20]. Therefore, there is need for toxicity test of the flower of *S. setigera*. The aim of this study is to determine the acute toxicity of methanolic extract of *S. setigera* (MESS) flower on selected organs, via blood chemistry and histopathology analysis using female wistar albino rats.

Figure 1: *Sterculia setigera* Del. Plant Field survey 2021

Figure 2: The flowers of *Sterculia setigera* Del.

MATERIALS AND METHODS

Chemicals and Drugs

Ketamine hydrochloride and Xylazine (Sigma-Aldrich, USA), being control drugs were obtained from Yobe State University Teaching Hospital Damaturu. Methanol (Loba Chemie India). Eosin and Haematoxylin were obtained from Pharmacy section of Yobe State University Teaching Hospital Damaturu. All relevant chemicals were of analytical grade.

Study Area

Fresh flower parts of *S. setigera* (Voucher number 103) were collected from Yobe State University Agric. Farm along Gujba Road longitude 11.6750^0N and latitude 11.9491^0E.

Collection and Authentication

The flowers were authenticated by Mr. Salihu Abdullahi (Taxonomist) at the Department of Biological Sciences, Yobe State University Damaturu. The sample was air dried under shade at ambient temperature, then crushed into powder using mortar and pestle, weighed and stored in tied polythene bag until required for analysis.

Sample Preparation

Sterculia setigera flower was air dry under ambient temperature and after drying it was powdered by laboratory mill, then weighed using weighing balance, soxhlet extractor was set up and the heating mantle was set at 64.7℃ which is the boiling point of methanol, 1000g of powdered sample was extracted exhaustively with 2.5L portions of methanol in soxhlet extractor. The procedure was repeated between each extraction to recover solvent and redistilled [22]. The volume of the extract was reduced to 100ml by simple distillation technique, after solvent was reduced to 100ml, the solvent containing extract was allowed to settle, the mixture was separated from the residue by filtering with Whatmann no. 1 filter paper and then kept in clearly labelled and weighed container to air dried. The container plus the extract was weighed, the drying and weighing continued at the interval of 48hours in order to obtain constant weight, after constant weight was obtained, the percentage (%) yield w/w was calculated to be 8.01% which was observed to be appreciable, its texture and colour were solid and deep brown respectively, the extract was kept in a drying cabinet prior to further analytical use.

Experimental Animals

This study was conducted using an experimental animal model. Healthy female Wistar albino rats weighing between 63-81g were obtained from Science Laboratory Technology Department, Federal Polytechnic Damaturu, Animal House.

Experimental Design

The rats were randomly distributed into five groups of three each fed on a diet of standard pellet Grand cereal (UAC) and distilled water. The animals were kept in marked cages at 28 ± 2 ˚C temperature and 50 ± 10% humidity, in a standard light/dark cycle (12h light/12 dark cycle). Administration of extract, blood and organ sampling as well as all surgical procedures were carried out with humane care according to good practice guide for the administration of substances and collection of blood, including the routes and volumes [22].

Acute Toxicity Study

The toxicity test was conducted using a slightly modified method of El-Ishaq *et al*. [22]. Fifteen female Wistar albino rats were distributed based on weight into five groups of three rats each. The animals were selected and marked on the fur to permit individual identification, kept in marked cages for a week with close observation prior to dosing to allow for acclimatization to the laboratory conditions and for detection of any noticeable abnormal behaviors. The rats were fasted for 4 hours before administration of extract, but water was allowed *ad libitum*. Group I served as normal control, administered with 2.0ml distilled water; group II, III, IV and V were orally administered crude extract dissolved in distilled water 5mg/kg BW, 50mg/kg BW, 300mg/kg BW and 1000mg/kg BW by intragastric route using gavage method. Wellness parameters of animals were observed continuously

during the first 30 min, 60 min, and periodically for the next twenty-four hours and then daily for fourteen days. All observations were systematically recorded.

The animals were fasted overnight prior to being sacrificed under anesthesia using ketamine (150mg/kg). blood from each animal of all groups were collected via cardiac puncture using a 3 ml syringe with 26G x ½ (0.45 x 13 mm) needle for biochemical analyses; alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), blood urea nitrogen (BUN), uric acid (UA), creatinine (CR) and total protein (TP). The remaining whole blood was collected in EDTA tubes for haematological parameters. The organs were examined for gross pathological changes and representative samples from the liver and kidney were collected in freshly prepared 10% buffered formalin for microscopic histopathology examination by cutting sections of 4-5µm thickness and stained with haematoxylin and eosin [22].

Statistical Analysis

All values are reported as mean ± standard error of the mean (SEM) and compared using one-way analysis of variance values were considered significant when ($p < 0.05$).

RESULTS

The percentage yield of crude extract of *S. setigera* flower is 8.01%. Toxicological study was carried out to check the safety of plant products for human use. Toxicity of substances affects the health of organism therefore, to ascertain the safety of plant based substances there is need to subject the plant product for toxicity analysis [18]; [23].

The results obtained are summarized in the table below, which include the effects of methanolic extract of *S. setigera* flower on body weight, organ weight, serum biochemistry and haematology parameters. Figures 3-10 below shows photomicrographs of liver and kidney of treated and untreated rats with MESS flower.

Effect of MESS on body weight gain and organ weight

The average weight gain of the treated groups was lower than that of the control group, with 5mg/Kg BW being the lowest (Table 1). However, the difference in the percentage of weight increment in the control and the treated groups were statistically significant. Table 2 shows no significant difference in the body and organs weight between control and treated groups.

Table 1: Effect of MESS on the body weight of treated rats

Treatment dose	Initial body wt (g)	Final body wt (g)	Mean body wt increase(g)	Wt gain (%)
Control 2.0ml DW	63.34 ± 3.38	107.93 ± 6.25	44.59	70.39a
5.0mg/kgBW	64.43 ± 3.32	84.06 ± 4.09	19.63	30.46b
50mg/kgBW	68.77 ± 2.47	96.00 ± 0.85	27.23	39.59b
300mg/kg BW	74.39 ± 0.74	112.06 ± 17.27	37.67	50.63b
1,000mg/kg BW	81.34 ± 4.19	118.66 ± 12.07	37.32	45.88b

Values are expressed as mean ± SEM, n=3 for each group. Key: wt= Body Weight
There is significant difference between control (a) and tested groups (b) ($p \leq 0.005$).

Table 2: Effect of MESS on organs weight of treated rats

Treatment dose	**Final body Wt (g)**	**Liver Wt (g)**	**Kidney Wt (g)**
Control 2.0ml	107.93 ± 6.25	4.9 ± 0.4	0.8 ± 0.1
5.0mg/kg BW	84.06 ± 4.09	3.8 ± 4.4	0.9 ± 0.05
50mg/kg BW	96.00 ± 0.85	3.7 ± 0.5	0.9 ± 0.0
300mg/kg BW	112.06 ± 17.27	4.5 ± 0.45	1.0 ± 0.1

1,000mg/kg BW	118.66 ± 12.07	5.3 ± 0.49	1.2 ± 0.0

Values are expressed as mean ± SEM, n=3 for each group, Key: wt= Body Weight
There is no significant difference in liver and kidney final weight between control and tested groups ($p \geq 0.005$).

Effect of MESS on Biochemical Parameters

Methanolic extract treated groups showed no significant difference in biochemical parameters such as ALT, ALP, Urea, and TP while Cr, AST and Uric acid showed significant difference between control and the treated groups (Table 3).

Table 3: Effect of MESS on biochemical indices of the treated and control rats

	Treatment				
Biochemical index	**Control**	**5.0mg/kgBW**	**50mg/kgBW**	**300mg/kg BW**	**1,000mg/kg BW**
ALT (µ/L)	795.5±77.2[a]	541.3±204.23[b]	681.5±82.9	630±98.63	366.6±151.74[b]
ALP (µ/L)	743±102.9[a]	860±51.33	590±52.3	902±29.70	719±182.60
AST (µ/L)	651±32.7[a]	533.6±183.41	557±95.5	582.3±138.35	245.3±225.62[b]
Cr (µmol/L)	16.5±2.0[a]	22±3.27[b]	35.5±7.8[b]	22±7.79[b]	27±9.42[b]
Urea (µmol/L)	6.3±1.1[a]	6.76±0.05	5±0.3	4.8±0.50	4.4±0.25
Uric acid(µmol/L)	599.5±45.3[a]	371±113.66	289±43.3	252±55.31	138.3±104.19[b]
TP (gm/L)	66.5±1.2[a]	62.66±1.25	57.5±1.2	58.6±1.25	58.3±2.62

Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Aspartate Aminotransferase (AST), Creatinine (Cr), Blood Urea Nitrogen (BUN), Uric Acid (UA), and Total Protein (TP).
Values are expressed as mean ± SEM, n = 3 for each group.
There is significance difference between some biochemical indices (b) and control (a) ($p \leq 0.005$) see table 3 for comparison.

Effect of MESS on Haematological Parameters

Methanolic extract activity on HCT showed a significant decrease ($P > 0.05$) between control and all treated groups. Furthermore, the MCV of 50mg/kg BW and 300mg/kg BW treated groups showed a significant decrease ($P > 0.05$) when compared to the control group. In addition, platelet counts and WBC of 5mg/kg BW treated groups showed a significant increase ($P < 0.05$) while 50mg/kg BW treated groups showed a significant decreased when compared to the control respectively. MCHC results for 50mg/kg BW and 300mg/kg BW groups were statistically increased significantly ($P < 0.05$). Meanwhile HGB, RBC, MCH and RDW did not show any statistical significance ($P > 0.05$) amongst the various groups.

Table 4: Effect of MESS on haematological parameters of the treated and control rats

		Treatment			
Haematological index	**Control**	**5.0mg/kgBW**	**50mg/kgBW**	**300mg/kg BW**	**1,000mg/kg BW**
HGB(g/dl)	8.5±1.3	10.3±0.42	11.25±1.0	9.83±0.70	11.86±1.13
HCT (%)	37.3±9.6	34.13±1.67	35.7±3.8	29.4±1.98	40.3±4.97
RBC (10^6/µl)	5.12±1.3	5.3±0.13	6.03±0.6	4.89±0.33	6.20±0.64
MCV (fl)	66.65±0.4	64.36±1.80	59.2±0.4	60.13±0.17	64.86±2.66
MCH (g/dL)	17.35±2.0	19.43±0.53	18.7±0.2	20.1±0.41	19.13±0.21
MCHC (g/dL)	26±2.8	30.2±1.36	31.6±0.5	33.46±0.78	29.56±1.58
RDW (%)	14.15±0.5	14.26±0.95	12.55±0.1	15.3±0.73	14.2±0.91
WBC (10^3/µl)	7.75±3.2[a]	15.66±2.90	4.3±0.4[b]	7.33±4.88	7.83±3.23

PLT (10^3/µl)	280±180[a]	369.33±111.52	131±55.5[b]	229.66±43.10	248±77.80

Hemoglobin (HGB), Hematocrit (HCT), Red Blood Cell (RBC), Mean corpuscular volume (MCV), Mean corpuscular Hemoglobin (MCH), Mean corpuscular Hemoglobin concentration (MCHC), Red Blood Cell volume distribution width (RDW), White Blood Cell (WBC), and Platelet (PLT). Values are expressed as mean ± SEM, n = 3 for each group

There is significance difference between WBC and PLT (b) and control (a) ($p \leq 0.005$) see table 4 for comparison.

Histopathology

Liver sections of the rats treated with methanolic extract of *S. setigera* at 5mg/kg BW showed normal hepatocytes arranged in tubular pattern, the portal triads and central vein are normal. 50mg/kg BW showed hepatic tissue disposed in lobular pattern and composed of hepatocytic cells arranged in trabeculae. There is mild periportal infiltration by inflammatory cells, 300mg/kg BW showed liver tissue with moderate periportal imflammatory cell infiltrates and focal mild microvesicular steatosis and 1000mg/kg BW is similar to 300mg/kg BW but no steatosis. For kidney sections, both control and treated groups even with the highest dose at 1,000mg/kg BW have normal glomeruli, tubules, interstitium and blood vessels.

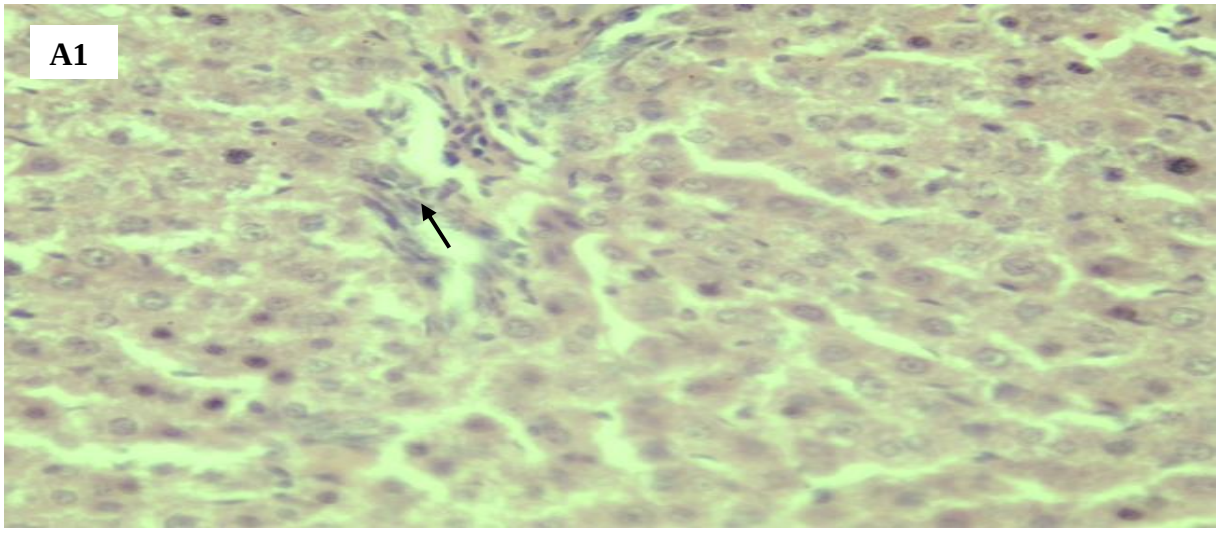

Figure 3: Portal triade: Photomicrograph of liver section shows normal hepatocytes arranged in tubular pattern, the portal triads is normal (H & E stain, magnification x40) (A1) control (dH_2O)

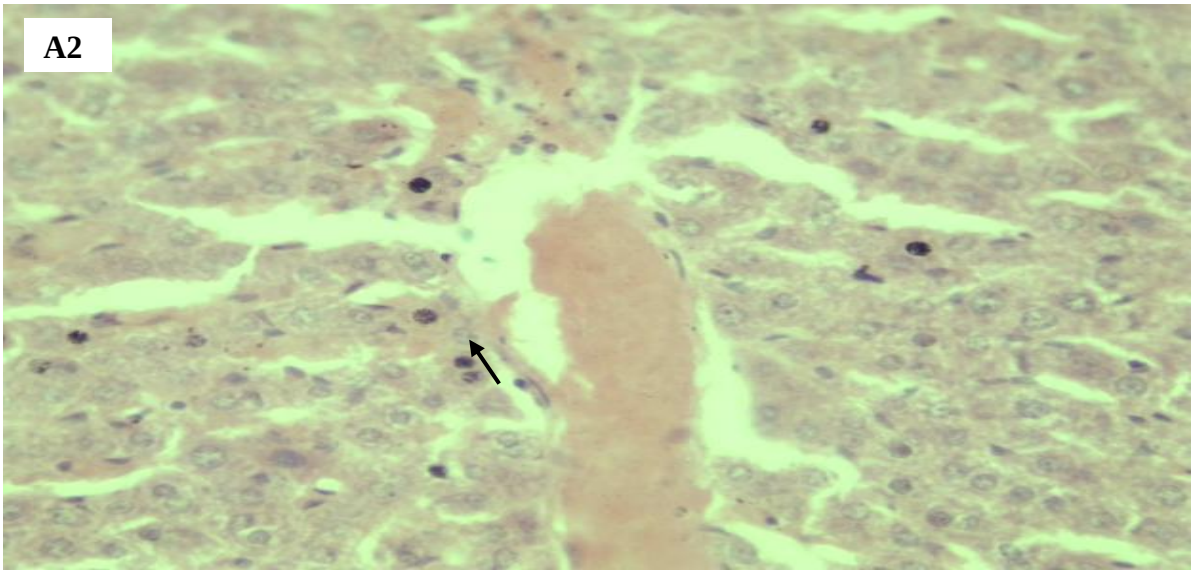

Figure 4: Central vein: Photomicrograph of liver section showing normal hepatocytes arranged in tubular pattern, the central vein are normal (H & E stain, magnification x40) (A2) control (dH_2O)

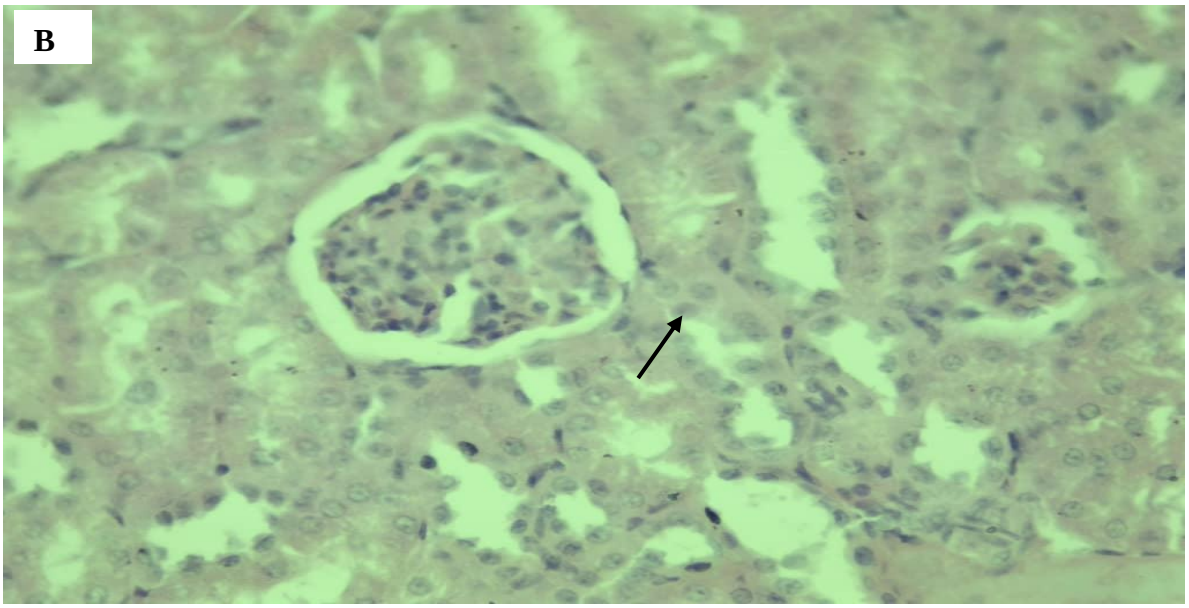

Fig. 5: Photomicrograph of liver section showing normal hepatocytes arranged in tubular pattern, the portal triads and central veins are normal (H & E stain, magnification x40) (B) 5mg/kg BW

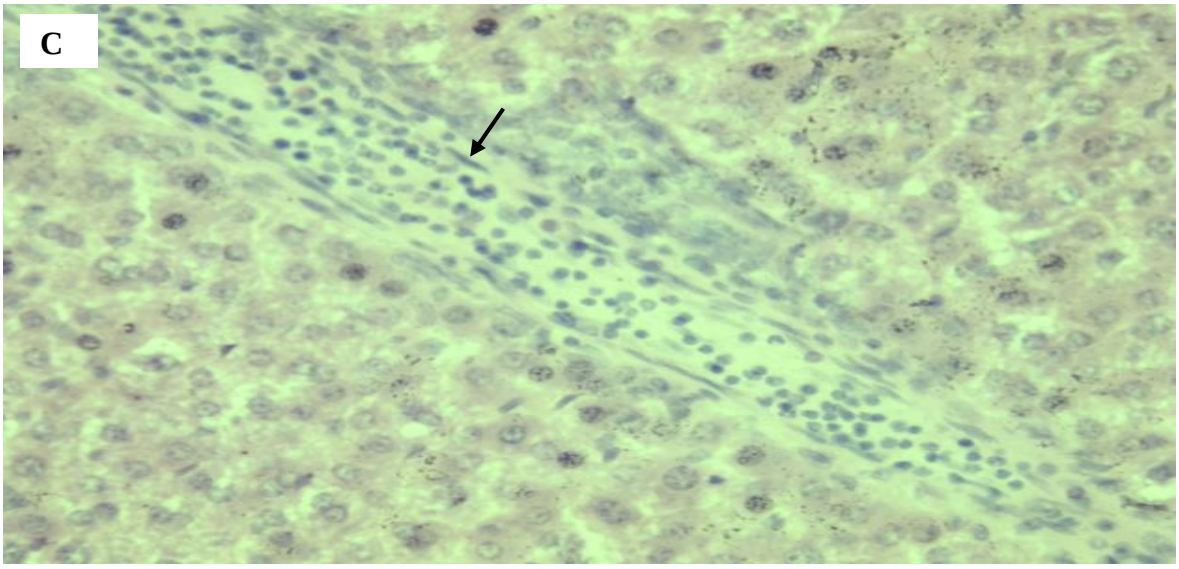

Figure 6: Photomicrograph of liver section shows hepatic tissue disposed in lobular pattern and composed of hepatocytic cells arranged in trabeculae with mild periportal infiltration by inflammatory cells, (H & E stain, magnification x40) (C) 50mg/kg BW

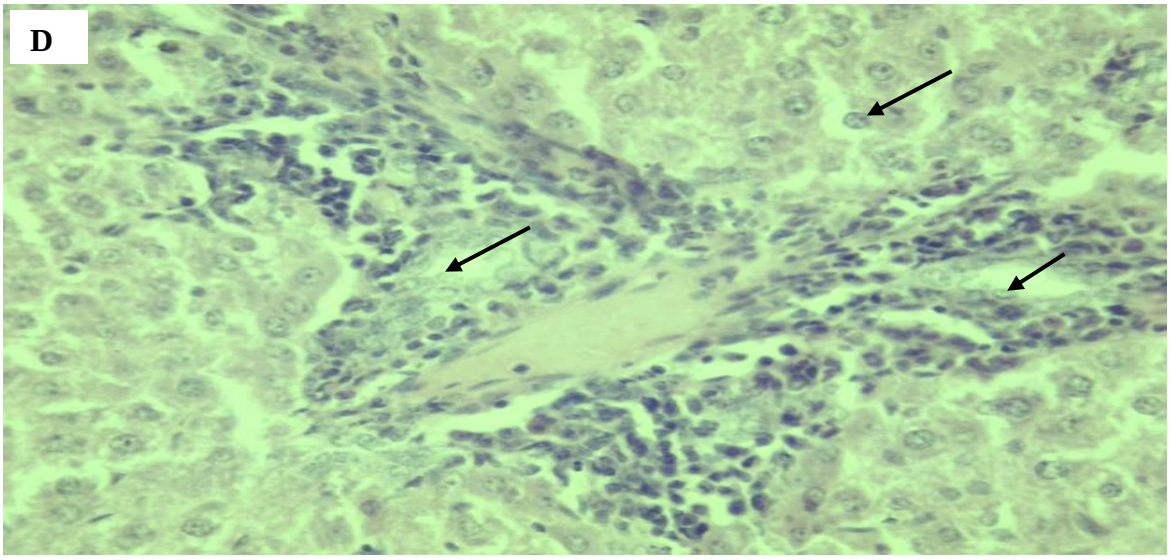

Figure 7: Photomicrograph of liver section shows liver tissue with moderate periportal inflammatory cell infiltrates and focal mild microvesicular steatosis. (H & E stain, magnification x40) (D) 300mg/kg BW

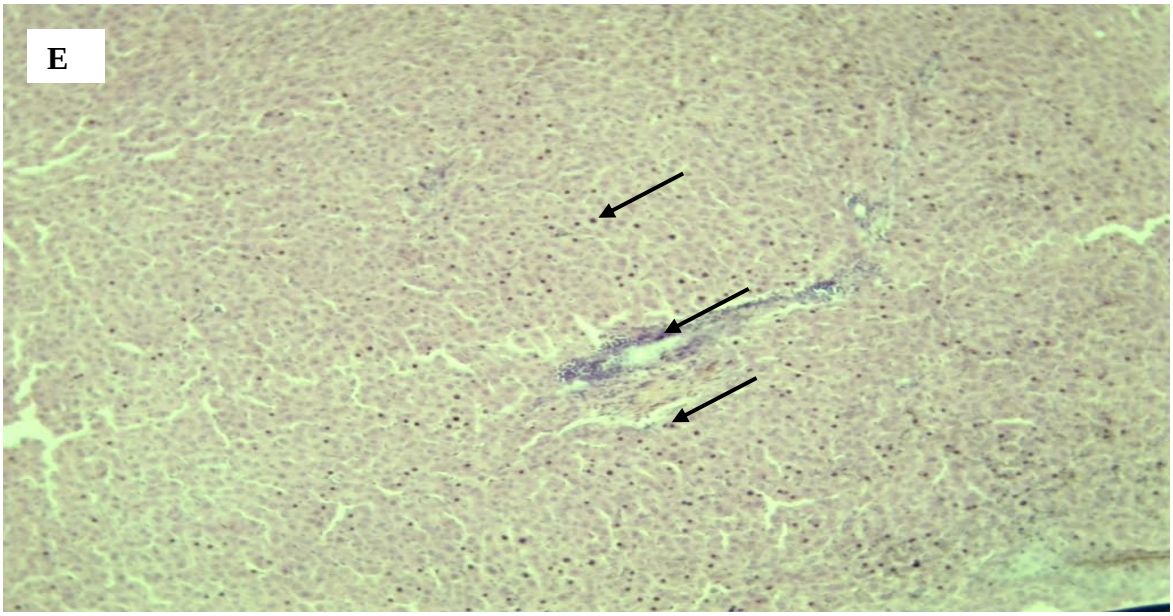

Fig.8: Photomicrograph of liver section shows liver tissue with moderate periportal inflammatory cell infiltrates but no steatosis. (H & E stain, magnification x10) (E) 1,000mg/kg BW

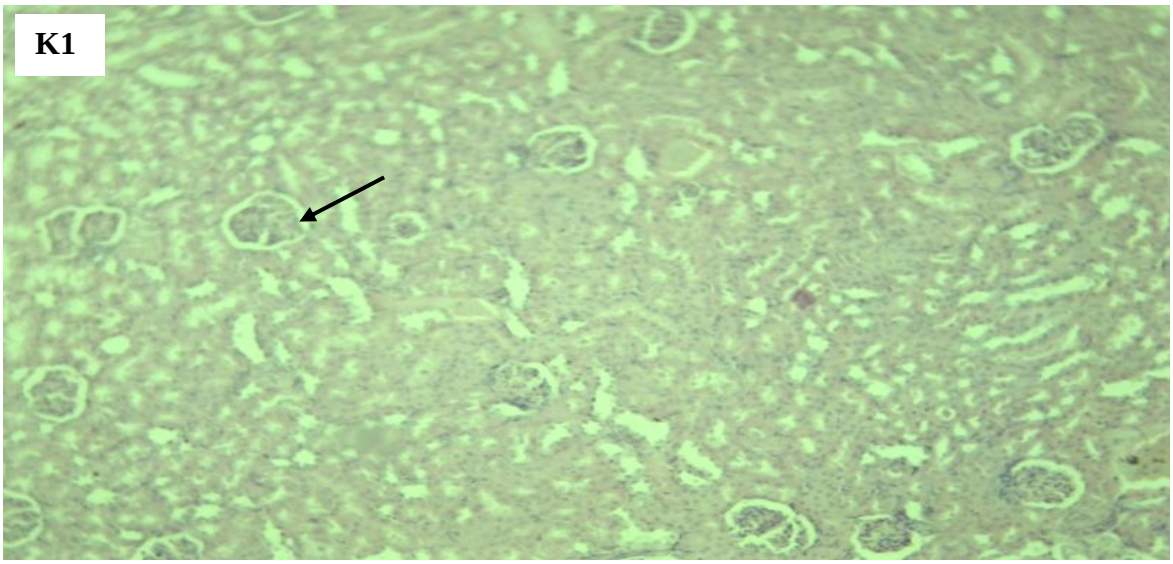

Fig.9: Photomicrograph of kidney section shows renal tissue composed of normal appearing cortex and medulla the glomeruli and tubules are unremarkable (H & E stain, magnification x40). (K1) control (dH_2O)

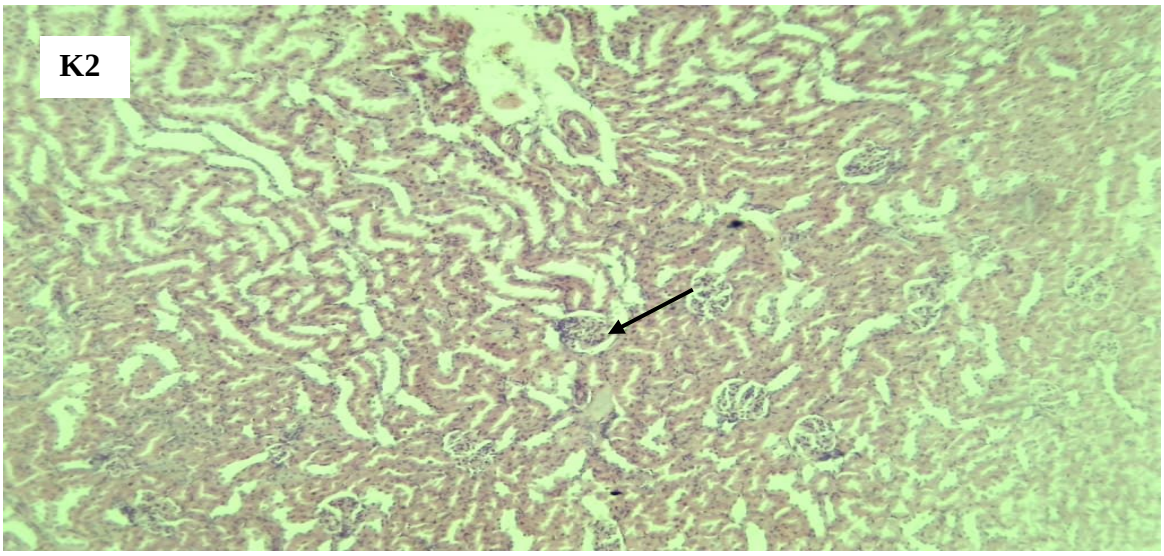

Fig.10: Photomicrograph of kidney section shows renal tissue composed of normal appearing cortex and medulla the glomeruli and tubules are unremarkable (H & E stain, magnification x40). (K2) 1,000mg/kg BW

DISCUSSION

In this study, the laboratory processed dried form of *S. setigera* flower was extracted using methanol, with a percentage yield of 8.01% of the initial weight. The obtained result was similar to the one obtained by [21] which is 7.98% and differed significantly with the result 5.65% reported by [31]. Acute toxicity study is invariably the first step in almost all screening investigation of herbal medicine of unknown potential. Most acute toxicity data are then used to predict safe dose limit in clinical application because some herbs exert harmful effects even at very low doses to sensitive tissues and organs in the body [22]. Hence multiple stages and doses studies are considered as one of the most valuable tools used in evaluating the biosafety profile of medicinal plants [22,24]; [25]. The flower extract of *S. setigera* was administered to wistar albino rats at doses of 5mg/kg BW, 50mg/kg BW, 300mg/kg BW and 1,000mg/kg BW for 14 days. Findings showed that there were no abnormal changes in the general appearance and no alteration in the behaviour of animals in the treated groups. Also, no mortality was recorded even in rats treated with higher dose of *S. setigera*. The mean percentage weight gain of rats in control group was 70.39% while 45.88% is the weight gain in group treated at higher dose (table 1). In this study, the effect of methanolic extracts on biochemical parameters reveals a significant increase in ALP and decrease in uric acid. Alkaline phosphate is an enzyme that mainly released into blood circulation by the liver and bones, at higher concentrations may be as a result of the mild liver damage caused by *S. setigera.* Histopathology findings of the liver confirmed this result and showed mild periportal infiltration by inflammatory cells and mild microvesicular steatosis.

Contrarily in this study, a significant increase was observed in a haematological parameter, such as MCHC ($P<0.05$) when compared between treated groups and control. Which may be due to the effect of the plant extract. However, literature have shown that the administration of medicinal plants can alter the normal ranges of haematological parameters [22,26]. Meanwhile WBC and PLT indices showed significant differences amongst the treated groups, whereas MCV, HGB, RBC, MCH, RDW and HCT were statistically insignificant ($P>0.05$) as compared to the control group. The difference observed in WBC count of the control and *S. setigera* flower extract-treated groups suggests that the plant does not possess toxins because the major functions of WBCs and its differential are to fight infections, defend the body by phagocytosis against invasion by foreign bodies or toxins, and produce or distribute antibody in immune response. Histopathology examination was conducted according to [22] and [27] Liver and kidney appeared normal and showed no markedly difference between control and treated rats. However, the livers of rats treated with methanolic extract showed mild periportal infiltration by

inflammatory cells and mild microvesicular steatosis. But no bile stasis. *S. setigera* methanolic extract of the flower did not cause any death or abnormal behaviours in the treated rats.

The presence of different phytochemicals in medicinal plants can be linked to several biological activities and alterations in the biochemical, haematological indices and histology pattern of the organs, especially on the liver and kidney. Phytochemical studies revealed that *S. setigera* stem bark, leaves and flowers contained several organically active metabolites such as terpenoids, polyphenol, saponins, steroids flavonoids, tannins and cardiac glycosides [12,11,23,28,32].

These metabolites may alter some of the haematological indices. Their presence in *S. setigera* flower extract might have different pharmacological and physiological effects on animal tissues or might act harmoniously to produce different biological and toxicological effect [29]. Furthermore, [16,13,14,30] have revealed the presence of anti-inflammatory in stem bark of S. *setigera* extract using male Sprague-Dawley rats, antituberclosis, antioxidant and antisickling respectively. Also the presence of bioactive compounds such as polyphenols, flavonoids, cardiac glycoside, terpenoids, steroid, tannins, and saponin were reported. The effective doses of *S. setigera* have been reported in the literature and varies from one study to another depends on the experimental model. For instance, anti-inflammatory of methanolic extract of *S. setigera* has been identified at 30-300mg/kg BW [16], antituberclosis doses has been reported at 62µg/ml [14]. Antioxidant, anti-sickling and anti-malarial effective doses of *S. setigera* have been carried out at doses less than 1,000mg/kg [13,30,31]. All these pharmacological effective doses are still less than the maximum dose (1,000mg/kg). In view of the fact that *S. setigera* is commonly used in traditional medicine and studies on different parts of the plant revealed the plant as potential source of bioactive compounds, possess important pharmacological activities and non-toxic [4,5,6]; [7,11,12,13,14,15,20]. Therefore, this study can be used as basis for the safety profile of this plant. The isolation of secondary metabolites in the flower extract will be the basis for further studies on the effect of this extract on body tissues.

CONCLUSION

The results from this study showed that *S. setigera* flower methanolic extract caused no behavioral abnormality, mortality or significant biochemical alteration in experimental animals, even though methanolic extract regulated some of the haematological indices. Therefore, it could be inferred that the extract may be safe up to 1,000mg/kg BW. The obtained result could be used to justify the safety of traditional application of the plant for treatment of different ailments, however further studies are needed to confirm these pharmacological activities and to investigate the fundamental mechanism of actions of the isolated bioactive components of this plant.

REFERENCES

[1]. Idyu II, Deshi EF, Idyu VC, & Ogundeko TO. The Anti-diarrhoeal Effect of Ethanolic –Bark Extract of *Sterculia setigera* in Mice. *Asian Journal of Science and Technology* 2015:6(5), 1397-1400.

[2]. Zaruwa MZ, Ibok NI, Ibok IU, Onyenonachi EC, Danchai C, Ahmed AG, Ahmed MU, Sudi IY. Effects of *Sterculia setigera*, Del. Stem Bark Extract on Hematological and Biochemical Parameters of Wistar Rats. *Biochem Insights*, 2016:9, 19-22.

[3]. El-khalifa AA. Domestication of *Sterculia setigera* (L.) in Sudan [*Ph.D Thesis*] University of Khartoum, 2007.

[4]. Mendham J, Denney RC, Barnes JD, Thomas M. Vogel Text Book on Quantitative Chemical Analysis (6th edition) Dorling Kindersley (India) Pvt Ltd, F.I.E Pataparaganji Delhi 110092, India, 2006: pp. 340-487, 612-656.

[5]. Isa PA, Hitler L, Joseph IA, & Oyetola O. Evaluation of Metals Concentration in Selected Medicinal Plants (*Sterculia setigera* Del. and *Sclerocarya birrea* (A. rich.) Hochst) Collected from Bwabul Spring, Bambuka and Jalingo Low-lands, Taraba State. *Journal of Environmental and Analytical Chemistry*, 2017:4(4), 2380-2391.

[6]. Chen YE, Yuan S, Su YO, & Wang L. Comparison of Heavy Metal Accumulation Capacity of some Indigenous Moses in Southwest China cities. *A Journal of Plant Soil Environment*, 2010:56, 60-66.

[7]. Khattak MI, Jabeen R, Hameed M, & Arfat Y. A study of some Heavy Metal Found: In medicinal plants (*Euphorbia cornigera, Rhazya Stricta* and *Citrullus colocynthis*) in Turbat Region of Balochistan with Reference to Prevention of Environmental Pollution. *Pakistan Journal of Botany*, 2015:47,1511-1516.

[8]. Gune A, Alpaslan M, Inal, A. Plant growth and fertilizer. *Ankara University Agriculture pub.* 1539 Turkey. 2004.

[9]. Alqasim AM, Gabriel O, & Is-Haq IU. Medicinal Plants Species Diversity and Access to Traditional Herbal Medicine Among the Samburu People *Journal of Medicinal Plants studies* 2013:1(5), 112-118.

[10]. Atakpama W, Pereki, H, Batawila K, Akpagana K. (2018). Ethnobotanical Knowledge of *Sterculia setigera* Del. in the Sudanian Zones of Togo (West Africa). *Revue Marocaine des Sciences Agronomiques Veterinaires*, 6(1):73-77.

[11]. Hamidu AA. Phytochemical Constituents of the Leaves of *Sterculia setigera*, *Journal of* Pharmacy, 2012:2(1), 062 – 064.

[12]. Tor-Anyiin TA, Akpuaka MU, & Oluma HOA. Phytochemical and Antimicrobial Studies on Stem Oluma Bark Extract of *Sterculia setigera* Del. *African Journal of Biotechnology*, 2011:10(53), 11011-11015.

[13]. Nahla MM, Taha A, & Barakat, MM. Antioxidant and Cytotoxic Activities of *Sterculia setigera* Del. *American Journal of Research Communication*, 2018:6(5), 41-49.

[14]. Babalola IT, Esther AA, Yuehong W, Francis OS. Anti-TB Activity of *Sterculia setigera* Del., Leaves *Journal of Pharmacognosy and Phytochemistry* 2012:1(3), 19-26.

[15]. Aishatu U, & Hamza AP. Isolation and Characterization of Anti-plasmodial Compound from *Sterculia setigera* delile *International Journal of Natural, Pure and Applied Science*, 2017:12, 1-7.

[16]. Henneh IT, Robertson A, Elvis OA, Daniels K, Geoge O, Bashiru A, Joseph A, Fred JE, & Francis T. Stem Bark Extract of *Sterculia setigera* Del. Exhibits Anti-inflammatory Properties Through Membrane Stabilization, Inhibition of Protein Denaturation and Prostaglandin E_2 Activity *Journal of Pharmaceutical Research International* 2018:22(5), 1-11.

[17]. Ogundeko TO, Idyu II, Deshi EF, Idyu VC. The anti-diarrhoeal effect of ethanolic-bark extract of *Sterculia setigera* in mice. *Asian Journal of science and Technology*, 2015:6(5):1397-1400.

[18]. Garba, MH, Sherifat ML, Abdul-majeed AO, Hafsa LM, Awal AB, SaaE adu AD, & Lekene BJ. Hepato-Protective Potentials of *Sterculia setigera* Stem Bark Extract on Acetaminophen Induced Hepatotoxicity in Wistar Albino Rats *Academic Journal*, 2018:12(29), 557-562.

[19]. Judith F, Ahounou A, Andre H, Geoffroy OB, Huguette A, Aldo R, Gnonlonfoun-SO, Joachim DG, & Pierre, HD. Laboratory of Pharmacognosy and Essential Oils, Faculty of Sciences and Techniques, University of Abomey-Calavi, 01 BP 918, ISBA Cotonou, Republic of Benin. 2009.

[20]. Muhammad A, Musa MI, & Adamu M. *In vitro* Screening of Potential Antioxidative and Toxicity of the Stem Bark Extracts from *Sterculia setigera* Del. *Algerian Journal of Natural Products* 2020:8(2), 774 – 779.
[21]. Gautam MK, Sing A, Rao CV, & Goel RK. Toxicological Evaluation of *Murraya paniculata* (Linn) Leaves Extract on Rodent. *American Journal of Pharmacology and Toxicology*, 2012:7(2), 62-67.
[22]. El-Ishaq A, Alshawsh MA, Mun KS, & Chik, Z. Biochemical and Toxicological Effects of Methanolic Extract of *Asparagus africanus* Lam in Sprague-Dawley rats. *Peer Journal* 2020, 8:e9138.
[23]. Ukwuani-Kwaja AN, Nwaogu J, Abba A, Yahaya M. Inhibitory Effects of Methanolic Stem Bark Extracts of *Sterculia setigera* and *Ficus platyphylla* on Hemoglobin Glycosylation and α-amylase. *Advances in Diabetes and Metabolism*, 2021:9(2), 13-18.
[24]. Abiodun HA, Oyinlade CO, Oluwatobi SA. Sub-Acute Evaluation of Extract of *Syzygium malaccense* in Albino Rats. *Research Journal of Medicinal Plant* 2015:9, 60-70.
[25]. Woode E, & Abotsi WK. Antinociceptive Effect of an Ethanolic Extract of the Aerial Parts of *Hilleria latifolia* (Lam.) H. Walt. (Phytolaccaceae). *Journal of Pharmacy and Bioallied Science* 2011:3, 384-396.
[26]. Attal AR, Otari KV, Shete RV, Upasani C, & Nandgude T. *Abrus precatorius* Linnaeus: A Phytopharmacological Review. *Journal of Pharmacy Research*, 2010:3, 2585-2587.
[27]. Theise ND. Liver Biopsy Assessment in Chronic Viral Hepatitis: A Personal, Practical Approach. *Modern Pathology*, 2011:S3-S14.
[28]. Akin-Osanaiye BC, & Yusuf MK. Phytochemical Screening and Antibacterial Activity of Leaves of *Sterculia setigera* Extracts. *Direct Research Journal of Biology and Biotechnology*, 2018:4(4), 40-45.
[29]. Kebede S, Afework M, Debella A, Ergete W, Makonnen E. Toxicological Study of Butanol Fractionated Root Extract of *Asparagus africanus* Lam. on Some Blood Parameter and Histopathology of Liver and Kidney in Mice. *BMC Research Notes*, 2016: 9:49.
[30]. Abdullahi B. Anti-Sickling Effect and Activity Guide Fractionation of *Dichrostachys cinerea* (Wight & Arn) Root and *Sterculia setigera* Leaf Methanolic Extracts on Human Sickle Red Blood Cells *In Vitro*, Dept. Of Biochemistry, Ahmadu Bello University Zaria. (*Online Project*). 2016.
[31]. Udegbunam RI, Asuzu UI, Kene ROC, Udegbunam SO, & Chinaka N. Anti-Nociceptive, anti-inflammatory and Antioxidant Effect of Methanolic Leaf Extract of *Sterculia setigera*. *Journal of Pharmacology and Toxicology*, 2011:6(5), 516-524.
[32]. Louis H, Akakuku OU, Linus MN, Innocent J, & Pigweh IA. Qualitative and Quantitative Phytochemical Analysis of *Sclerocarya birrea* and *Sterculia setigera* in Kem and Yola, Adamawa State, Nigeria. *American Journal of Biomedical Research*, 2018:6(1), 1-10.
[33]. Atakpama W, Batawila K, Wala K, Douma M, Pereki H, Wala K, Dimobe K, Akpagana K, Gbeassor M. Ethnobotanical Knowledge of *Sterculia setigera* Del. In the Sudanian Zone of Togo (West Africa). *ISRN Botany* 2012:723157.
[34]. Maigari UA, & Hamza AP. Isolation and Characterization of Anti-Plasmodial Compounds from *Sterculia setigera* Delile. *International Journal of Natural Pure and Applied Sciences*, 2017:12(3), 1-7.