World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Research Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 4
Page: 453-471

PHYTOCHEMICAL, ANTIOXIDANT AND TOXICOLOGICAL ASSESSMENT OF *PERICOPSIS LAXIFLORA* (BAKER) STEM BARK EXTRACT IN RATS

Frederick Sarfo-Antwi[1*], Christopher Larbie[2], Benjamin Obukowho Emikpe[3], Regina Appiah–Opong[4], Daniel Seifu[5]

[1,5]Department of Biochemistry, School of Medicine, University of Global Health Equity, Butaro, Rwanda.
[2]Department of Biochemistry and Biotechnology, College of Science, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
[3]Department of Pathobiology, School of Veterinary Medicine, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.
[4]Department of Clinical Pathology, Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, Accra, Ghana.

Article Received: 26 June 2025 | | Article Revised: 17 July 2025 | | Article Accepted: 10 August 2025

***Corresponding Author: Frederick Sarfo-Antwi**
Department of Biochemistry, School of Medicine, University of Global Health Equity, Butaro, Rwanda.
DOI: https://doi.org/10.5281/zenodo.16889010

How to cite this Article: Frederick Sarfo-Antwi, Christopher Larbie, Benjamin Obukowho Emikpe, Regina Appiah-Opong, Daniel Seifu (2025) PHYTOCHEMICAL, ANTIOXIDANT AND TOXICOLOGICAL ASSESSMENT OF PERICOPSIS LAXIFLORA (BAKER) STEM BARK EXTRACT IN RATS. World Journal of Pharmaceutical Science and Research, 4(4), 453-471. https://doi.org/10.5281/zenodo.16889010

ABSTRACT

The study was aimed at evaluating the acute and subacute toxicity of the 50% hydroethanolic extract (HSE) and methanolic extract (MSE) of *Pericopsis laxiflora* stem bark. The extracts were analysed for phytochemical constituents, DPPH scavenging activity, FT-IR, and GC-MS using standard methods. The acute toxicity was assessed at a single oral dose of 5000 mg/kg body weight (b.wt.) of extract while in the subacute study, the extracts were administered orally (at doses of 100, 250, and 500 mg/kg, b,wt.) for 28 days and observed for signs of toxicity. Safety was assessed based on the effect of treatment on body weights, organ weights, haematology, serum biochemical indices, and histopathological examination of the liver. The extracts contained alkaloids, polyphenols, saponins, and cyanogenic glycosides with significant radical scavenging activity. The LD_{50} was established to be greater than 5000 mg/kg while the subacute study showed no significant effect on the body weights, organ weights, biochemical, and haematological parameters at all doses compared with non-treated animals. However, an increase in WBC levels was recorded in both sexes. No significant hepatic lesions were observed in histology. The present study showed that *Pericopsis laxiflora* stem bark hydroethanolic and methanolic extracts possess antioxidant properties and did not produce any harmful effect in both acute and sub-acute studies of male and female rats, therefore usage of these extracts for their medicinal purpose is recommended.

KEYWORDS: Toxicity, biochemical, histopathological, *Pericopsis laxiflora*.

INTRODUCTION

Plant-derived drugs are found in all civilizations and societies, so plants have long played a vital role in healthcare systems around the globe. In some developed nations, especially China and India, indigenous herbal medicine is part of the traditional and prevailing healing therapy. These remedies are socially permissible, commercially sustainable, and for the most part, are the only feasible source.[1] Therefore, plants used in herbal medicine have a vital role to play in the preservation of well-being around the world. Religious healers have used herbal and animal remedies since ancient times to preserve health and cure diseases. These medicines are widely used in Africa and Asia, including Ghana. Due to adverse side effects and the emergence of resistance to synthetic drugs, the use of plant-derived drugs is becoming increasingly common in developed countries.[2] However, recent surveys have shown that several medicinal plants have also demonstrated adverse effects.[3] This raises questions about the possible harmful impact of chronic use of such plants. Therefore, determining the toxicological effects of many medicinal plants extract intended for therapeutic or preclinical application is a vital part of the evaluation for safety and subsequent approval.[4] The choice of herbal products for therapy includes affordability, availability, and the perception that plants are less toxic than conventional medicines.[5] It is worth noting that plants are a major source of conventional drugs, including artemisinin, vincristine, and vinblastine from *Artemisia annua* and *Catharanthus roseus*, respectively. According to the World Health Organization, nearly 80% of the population in developing countries depend on traditional medicine for health care.[6]

Pericopsis laxiflora is one of the most popular and well-known plants with a long history of use among the Ghanaian population to treat jaundice and body weakness.[7] However, there is a dearth of information on its acute and subacute toxicity and antioxidant properties. Ongoing studies aimed at assessing the acute and chronic hepatoprotective effect were expedient to provide the scientific basis for its use. The current report focuses on the phytochemical, antioxidant, and toxicological assessment of *P. laxiflora* stem bark hydroethanolic extract (HSE) and methanolic extract (MSE) with the sole aim of advising its use in humans for the treatment of different diseases.

2. MATERIALS AND METHODS

2.1 Collection and authentication of plant materials

In February, 2025, *P. laxiflora* fresh stem bark was collected from healthy, fully grown plants from the Ejura Savannah forest reserve located in the Ashanti region of Ghana. They were authenticated at the University for Development Studies, School of Pharmacy and Pharmaceutical Sciences, Department of Pharmacognosy and Herbal Medicine, and a voucher specimen (UDS-SPPS/DP1/2025/L010) was deposited at the herbarium.

2.2 Extraction

The stem bark was cut into pieces, washed, dried under shade, and milled into a powder. One hundred grams of the powder was extracted with 500 mL of 50 % ethanol and methanol at room temperature with shaking for 24 hours. The extracts were then filtered through cotton wool and concentrated under 60°C pressure using a rotary evaporator (Buchi R205, Switzerland). They were transferred into sterile containers and freeze-dried to obtain the *Pericopsis laxiflora* hydroethanolic extracts (HSE) and methanolic extract (MSE). The extracts were re-dissolved in normal saline at the respective doses and used for the study.

2.3 Extract characterization

2.3.1 Phytochemical analyses

P. laxiflora stem bark extracts were analyzed for phytochemical constituents using standard procedures.[8] Phytochemicals tested for included alkaloids, flavonoids, cyanogenic glycosides, triterpenes, saponins, polyphenols, tannins, reduction sugar, anthracenosides, and phytosterol.

2.3.2 1, 1-Diphenyl-2-Picrylhydrazyl (DPPH) scavenging activity

The effect of HSE and MSE on DPPH radical was estimated using standard methods.[9] Briefly, an aliquot of extract (50-500 mg/mL) was added to a methanolic solution of DPPH (1 mM, 1 mL) and 4 mL of distilled water. The mixture was shaken and left to stand for 30 minutes at room temperature. The absorbance of the resulting solution was measured at 517 nm. As standard, ascorbic acid (50 µg) was used. The activity of radical scavenging (RSA) was calculated as the percentage decolouration of DPPH.

$$\% \text{ RSA} = \frac{[\text{Absorbance of blank } (OD_0) - \text{Absorbance of test } (OD1_)] \times 100}{\text{Absorbance of blank } (OD_0)}$$

2.3.3 Estimation of total phenolic content (TPC)

The total phenolic content of the extracts was assessed by the Folin Ciocalteu (FC) procedure[10], with some modifications. Approximately 0.1 g of the extract was dissolved in 5 mL of 0.3% HCl in methanol/water (60:40, v/v). The blend was allowed to stand for 5 minutes and added to 2 mL of 2 % Na_2CO_3. After 2 minutes, 50% Folin-Ciocalteau reagent (100 µL) was added to the mixture, then left for 30 minutes. Absorbance was measured at 750 nm against gallic acid as standard. All extracts were analysed in triplicate. Gallic acid standards (0.2, 0.4, 0., 0.8, and 1 mg/mL) were used to prepare the calibration curve. The overall phenolic content was calculated from standard curve and results were expressed as mg GAE/100g DM.

2.3.4 Estimation of total flavonoid content (TFC)

The determination of TFC was by the colorimetric method of aluminium chloride ($AlCl_3$), using gallic acid (10-100 mg/L) as a standard.[10] Briefly, 1.5 mL of 95% methanol, 100 µL of 10% $AlCl_3$, 100 µL of 1 M potassium acetate, and 2.8 mL of distilled water were mixed with 500 µL of the 1:20 diluted and filtered extract (at the original 100 mg/mL concentration in methanol). The mixture was incubated for 40 minutes at room temperature, and the absorbance was read at 415 nm. The TFC was expressed as mg/g dry weight of quercetin equivalence.

2.3.5 Estimation of Total Tannins (TT)

The amount of tannins in plant extracts was determined by a slightly modified Folin-Ciocalteu method.[11] To 5 µL of distilled water, 500 µL of Folin-Ciocalteu reagent, and 1 mL of 35% Na_2CO_3 solution were added followed by 0.5 g of extract. The mixture was well shaken and held for 30 min at room temperature. Gallic acid standard solutions (0.2, 0.4, 0.6, 0.8, and 1 mg/mL) were prepared in the same manner as previously described. The test's absorbance and solutions were measured at 725 nm. The calibration curve determined the total tannin content, and the results expressed the tannin content in terms of mg GAE / g DM.

2.3.6 FTIR analysis

The Fourier transform-infrared (FTIR; Shimadzu 8400S) was used to assess the functional groups contained in extracts. Samples were packed with KBr pellets, and the infrared spectra were recorded. The functional groups present were determined by comparing spectra with standard IR tables.[13]

2.3.7 Gas Chromatography-Mass Spectrometry (GCMS) spectra analyses

The extracts (HSE and MSE) were analysed using the GC-MS to identify the major compounds present. GC-MS analyses of the samples were performed using a PerkinElmer GC Clarus 580 Gas Chromatograph interfaced to a Mass Spectrometer PerkinElmer (Clarus SQ 8 S) with column and conditions previously described.[14] The total GC/MS running time was 50 min. Interpretation of mass-spectrum GC-MS was conducted using the National Institute of Standard and Technology (NIST) database, having more than 62,000 patterns.

2.3.8 Heavy Metal Analyses

One gram (1.0 g) of each of the samples was weighed into a 50 mL digestion tube. The sample was mixed with 1.0 mL of H_2O, 2.0 mL of conc. HCl, 5 mL of 1:1 conc. HNO_3: 60% $HClO_4$ and 2.0 mL of conc. H_2SO_4. The mixture was allowed to stand for, 20 minutes and then heated at 150 °C on a digestion block. Digested samples were allowed to cool and diluted to 50 mL mark with distilled. The digests were analysed using an Atomic Absorption Spectrometer (Analytikjena nova 400P) lead, copper, nickel, zinc, and iron.[15]

2.4 Toxicity Assessment

2.4.1 Animals

Healthy adult male and female Sprague Dawley rats (age < 8-12 weeks: body weight, 150-200g (male); 120-150 g (female)) were used to evaluate the subacute toxicity studies while albino mice (either sex;, 20 – 30g) were used for the acute study of HSE and MSE. Animals were obtained from the University of Ghana Medical School, Legon Accra, and housed in polypropylene cages suitably lined with wood shavings. Before testing, they were acclimatized in the animal holding facility of the Department of Biochemistry and Molecular Medicine, for two weeks, maintained under standard conditions (temperature 25±2 °C; relative humidity 65 percent; light/dark cycle 12/12h). The animals were fed with standard rat pellet feed (Agricare, Kumasi), and drinking water was supplied with stainless steel sipper tubes in clean polypropylene bottles *ad libitum*. They were marked solely on their tails using permanent markers for quick identification. All animal experiments were performed in compliance with the recommendations of the Committee for the Monitoring and Control of Animal Experimentation.[16]

2.4.2 Acute oral toxicity (single-dose oral toxicity study – OECD 425)

The OECD guidelines 425 was adapted in the acute oral toxicity study of HSE and MSE using albino mice (either sex;, 20 – 30g; n=6). HSE and MSE at maximum dose of 5000 mg/kg body weight (b.wt.) was dissolved in normal saline and administered by gavage (p.o.). Following the administration of extracts, the mortality of rats if any was observed. Further, signs of toxicity and behavioural changes were monitored every 4 h for 7 days.[17,18]

2.4.3 Sub-chronic oral toxicity of extracts (repeated dose 28-day oral toxicity study in rodents – OECD 407)

The OCED guideline 407[19] was adopted for the sub-chronic toxicity evaluation of HSE and MSE.

2.4.3.1 Experimental design

Thirty-five (35) male (150-200 g) and 35 female rats (120-150 g) were divided into fourteen groups and treated for 28 days (n=5). Table 1 shows the description of groups and treatment. All animals were fasted 12 hours before the first oral drug administration and had free access throughout the experiment to food and freshly distilled water. The animals were observed for signs of toxicity and mortality, including paw-licking, respiratory distress with stretching, diarrhoea, and death.

All animals were sacrificed on the 29th day following cervical decapitation. The animals were quickly slit at the neck, and blood samples were collected into gel activated tubes for biochemical analyses and EDTA tubes for haematological analyses.

2.4.3.2 Effect of treatment on body weight of animals

During treatment, individual body weights of all animals were recorded on the first day (Do) and end of every fourth day (D4, D8, D12, ……. and D28).

The percent change in body weight was calculated using the formula:

$$\%\ Change\ in\ Body\ Weight = \frac{Weight_n - Weight_o}{Weight_o} \times 100$$

Where, Weight n is the weight on D4, D8, D12, D16, D20, D24 and D28 and Weight $_o$ is the weight on the first day (D_0).

2.4.3.3 Effect of treatment on organ weights of rats

The liver, the kidney, the heart, the stomach, the spleen, the lung, the testes (male), and the uterus (female) were collected and rinsed in a buffered saline solution, dried on tissue paper, grossly observed, and weighed to obtain the absolute organ weight (AOW). The Relative Organ Weight (ROW) of each organ was calculated the formula:

$$ROW\% = \frac{AOW}{Body\ weight\ at\ sacrifice} \times 100\%$$

2.4.3.4 Effect of treatment on Haematological Parameters of rats

An automatic haematological analyser (Sysmex XS-1000i) was used to analyse the haematological profile of animals including haemoglobin (HB), white blood cell count (WBC), red blood cell count (RBC), haematocrit (HCT), platelets (PLT), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), and differential leucocyte count (neutrophils, lymphocytes, eosinophils, monocytes). Non-invasive markers of inflammation such as platelet lymphocyte ratio (PLR), neutrophil lymphocyte ratio (NLR), and PLR+NLR ratios were calculated.

2.4.3.5 Effect of treatment on some biochemical parameters

Blood samples in activated gel tubes were allowed to clot and centrifuged at 1500 g for 15 min to obtain blood serum. The following biochemical parameters were assessed: glucose, creatinine, urea, sodium, potassium, chloride, total protein, albumin, globulin, total bilirubin (TBil), direct bilirubin (DBil), alanine transaminase (ALT), aspartate transaminase (AST), triglyceride (TG), and cholesterol (total cholesterol, HDL cholesterol, LDL cholesterol) using an automated biochemistry analyser (ADVIA 2400, Siemens Healthcare) with reagents.

2.4.3.6 Histopathological Studies

The excised liver of animals was fixed in 10% buffered formalin (pH 7.4) and histologically processed. Five microliter sections were cut, stained with haematoxylin-eosin (HE) and tissues examined blindly by a pathologist, microscopically and photomicrographs were taken.

2.5 Statistical Analysis

All statistical data were presented as mean ± SEM and analysed using GraphPad Prism for Windows version 8.0 (GraphPad Software, San Diego, CA, USA) with a one-way analysis of variance test followed by Tukey Multiple Comparison Test, at 95% confidence interval.

3. RESULTS

3.1 Preliminary Phytochemical Screening

HSE and MSE after complete drying yielded 38% and 28%, respectively. Preliminary phytochemical screening of HSE and MSE revealed the presence of major phytochemical groups as shown in Table 2.

3.2 Quantitative Phytochemical constituent and radical scavenging activity

Table 3 shows the total contents of phenols (TPC), tannins (TTC), flavonoids (TPC), and DPPH scavenging activity (IC_{50}) of crude extracts. Extracts were rich in phenols, tannins, flavonoids and significant DPPH scavenging activity with HSE recording the highest.

3.2 FTIR Spectroscopic Analysis of *P. laxiflora* Extracts of stem bark

FT-IR spectra of HSE and MSE are shown in Table 4. The HSE and MSE possessed a broad peak representative of phenols and alcohols along with other functional groups.

3.3 Gas Chromatography-Mass Spectrum Analyses of Extracts

Various compounds were detected in the crude extracts of *P. laxiflora*. They included cycloheptasiloxane, phenol, hexadecanol, pentadecanone, and oleic acid (Figures 3 and 4; Tables 8 and 9).

3.4 Heavy Metal

Table 7 shows the presence of heavy metals in both the raw plant material and crude extracts. Low concentrations of Iron (Fe) and Zinc (Zn) were observed in the raw stem bark. However, they were below the detection limit (0.0001 ppm) in both HSE and MSE.

3.5 Acute Toxicity Study

No death was observed within 12 hours of continuous monitoring in the acute toxicity investigations, nor after 7 days. Physical traits (hair, skin, eyes, and nose) seemed normal. There was no salivation, diarrhoea, lethargy, or strange behaviour. The LD_{50} could be estimated to be $\geq$ 5000 mg/kg thus making it safe.

3.6 Subacute Toxicity Study

Over a 28-day, no fatalities were observed in rats administered HSE or MSE at dosages of 100, 250, and 500 mg/kg b.wt. through oral gavage. Throughout the study period, none of the animals (both male and female) displayed any visible morbidity or clinical indications of poisoning, such as changes in skin and hair, eyes, respiration rate, autonomic (salivation, sweating, and piloerection), or stereotypical behaviours.

3.6.1 Treatment effect on body weight

There was an increase in body weight in normal and treated groups, both male and female. The normal group had the most significant weight increases in both sexes (Figure 5). At termination, male and female animals receiving 100 and 250 mg/kg HSE respectively recorded the highest weight gain (Table 8).

3.6.2 Effect of treatment on relative organ weight

There was no significant effect of treatment on the relative organ weights of the rats for both sex after administration of HSE or MSE (Table 9).

3.6.3 Effect of treatment on haematological parameters

The were no significant changes haematological parameters in control and treated rats except for the white blood cell count (WBC), which in both extract treatments recorded an increase in all groups (Tables 10 and 11). The effect of treatment on some non-invasive markers of inflammation including platelet lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), and PLR+NLR ratios are presented in Table 12. Treatment did not induce inflammation in animals as shown.

3.6.4 Effect of treatment on biochemical parameters

Tables 13 and 14 show the effects of treatment on some biochemical markers to detect the state of some organs. No significant differences were observed in the parameters for both extracts and at all doses indicating the safety of extract (at all doses and sexes) on the liver, heart, kidneys, and lipid metabolism.

3.6.5 Effect of treatment on liver histology

Figure 7 shows the effect of treatment on liver histology. No major pathological alterations were observed in the gross and histopathological examination of the liver.

Table 1: Grouping and Treatment of animals in subacute study

S/N.	Group	Treatment
Male		
1	Normal control	Treated with potable water p.o (1 mL/kg body weight; b.wt)
2	100 mg HSE	Treated with 100 mg/kg b.wt of HSE
3	250 mg HSE	Treated with 250 mg/kg b.wt of MSE
4	500 mg HSE	Treated with 500 mg/kg b.wt of HSE
5	100 mg MSE	Treated with 100 mg/kg b.wt of MSE
6	250 mg MSE	Treated with 250 mg/kg b.wt of HSE
7	500 mg MSE	Treated with 500 mg/kg b.wt of HSE
Female		
8	Normal control	Treated with potable water p.o (1 mL/kg body weight; b.wt)
9	100 mg HSE	Treated with 100 mg/kg b.wt of HSE
10	250 mg HSE	Treated with 250 mg/kg b.wt of MSE
11	500 mg HSE	Treated with 500 mg/kg b.wt of HSE
12	100 mg MSE	Treated with 100 mg/kg b.wt of MSE
13	250 mg MSE	Treated with 250 mg/kg b.wt of HSE
14	500 mg MSE	Treated with 500 mg/kg b.wt of HSE

Table 2: Phytochemical constituents of *P. laxiflora* crude extract

Phytochemicals	HSE	MSE
Alkaloids	++	++
Anthracenoside	+	-
Polyphenols	++	+
Flavonoids	++	+
Triterpene	+	+
Cyanogenic Glycosides	++	+
Tannins	+	+
Saponins	++	+
Reducing sugar	+	-
Phytosterols	+	+

Key: Absent (-); Present in low concentration (+); Present in moderate concentration (++). Present in high concentration (+++).

Table 3: Quantitative Phytochemical constituent and radical scavenging activity of extracts.

Test	HSE	MSE	Vitamin C
Total Phenol (mgGAE/g)	25.23 ± 1.54	20.41 ± 2.34	
Total Tannin (mgGAE/g)	15.96 ± 3.13 [a]	8.25 ± 1.84 [a]	
Total Flavonoid (mgQ/g)	14.68 ± 2.75 [a]	9.28 ± 2.14 [a]	
DPPH (mg/mL)	0.48 ± 0.03 [a]	0.14 ± 0.02[a]	0.10 ± 0.04

Values represent the means of triplicate experiments. Statistical significance; "a" p<0.05-0.05-0.001 among extracts.

Table 4: FTIR Peak Values of *P. laxiflora* stem bark extract.

Peak No.	Wave Number (cm^{-1})	Functional Groups
HSE		
1	3265.68	Alcohol, Phenol
2	2920.09	Alkanes
3	2851.13	Aldehydes
4	1560.49	Nitro compound
5	1399.22	Alkanes
6	1108.03	Aliphatic amines
7	1032.01	Aliphatic amines
8	786.14	Aromatics
9	616.00	Alkyl halide
10	466.57	Alkyl halide
MSE		
1	3351.54	Alcohol, Phenol
2	2908.68	Alkanes
3	2180.16	Alkynes
4	1633.53	1^{o} Amines
5	1553.98	Nitro compounds
6	1454.33	Aromatics
7	1343.72	Nitro compounds
8	1019.80	Aliphatic amines
9	924.25	Carboxylic acids
10	462.95	Alkynes

Table 5: GC-MS analyses showing compounds present in HSE.

Peak	RF	Area	Area %	Norm %	SI	COMPOUNDS
1	24.57	3,80,571.5	1.304	5.768	95.42	Cycloheptasiloxane
2	25.15	2534896.2	1.242	5.254	96.37	Phenol
3	26.67	4249132.0	0.793	4.793	95.12	Cyclotasiloxane
4	27.86	6440336.5	1.203	5.203	92.32	Dodecanol
5	29.07	3539013.5	0.661	3.661	94.67	Phytol
6	29.13	4022554.5	0.751	4.751	86.72	Hexadecanol

7	30.00	4144050.0	0.774	4.774	92.68	Toluene-4-sulfonyloxy
8	31.83	4846425.0	0.905	4.905	94.36	Oleic acid
9	32.68	3960120.0	0.740	4.740	97.56	Estra-1, 3, 5 (10)-trien-17β-ol
10	33.96	6047608.5	1.129	5.129	96.78	Hexadecanoic acid

Table 6: GC-MS analyses showing compounds present in MSE.

Peak	RF	Area	Area %	Norm %	SI	COMPOUNDS
1	24.56	3,80,416.2	1.299	6.35	96.15	Cycloheptasiloxane
2	27.86	4267117.7	1.342	6.45	94.75	1-hexadecanol, 2-methyl
3	29.07	4325177.2	1.243	6.27	96.56	Tetramethyl-2-hexadecenol
4	30.00	4022554.5	0.751	4.25	86.72	Hexadecanoic acid
5	31.73	4144050.0	0.774	4.39	90.69	3-Isopropyl
6	32.62	3658712.5	0.605	3.43	95.07	Oleic acid
7	33.97	6254763.6	1.253	6.30	92.36	13-Octadecenoic acid
8	35.07	4236587.1	0.853	4.98	87.58	Estra-1,3,5-trien-17β-ol
9	37.01	5268943.4	1.254	6.30	96.71	Glycidol
10	38.01	4365721.6	1.142	5.53	98.34	2,3-Dihydroxypropyl

Table 7: Heavy metal content of raw stem bark plant material, HES and MSE.

Sample	Concentration (mg/L)				
	Fe	Zn	Ni	Cu	Pb
Stem Bark Raw	0.009 ± 0.00	0.004 ± 0.00	BDL	BDL	BDL
HSE	BDL	BDL	BDL	BDL	BDL
HSE	BDL	BDL	BDL	BDL	BDL

Values are expressed as mean ± SEM (of 3 determinations), BDL: Below the Detection Limit; Iron (Fe), Zinc (Zn) Lead (Pb), Copper (Cu), and Nickel (Ni)

Table 8: Effect of Treatment on Body Weight at Termination.

	% Change in Body Weight	
Treatment	***Male***	***Female***
Normal	52.64±5.85	49.40±2.24
HSE 100 mg/kg	30.78±1.04[a]	30.87±1.12[a]
HSE 250 mg/kg	48.42±2.28	25.01±0.72[a]
HSE 500 mg/kg	34.73±1.49[a]	26.97±1.52[a]
MSE 100 mg/kg	33.65±4.74[a]	25.01±0.69[a]
MSE 250 mg/kg	33.79±2.48[a]	21.61±2.59[a]
MSE 500 mg/kg	33.10±2.67[a]	21.90±1.35[a]

Each values represent a mean±SEM (n=5). Statistical significance: "a" p<0.05-0.05-0.001 compared with normal.

Table 9: Effect of treatment on relative organ weights in male and female animals.

Organ Weight (%)	Normal	Treatments					
		HSE			MSE		
		100 mg	250 mg	500 mg	100 mg	250 mg	500 mg
Male							
Liver	5.70 ± 0.61	5.52 ± 0.74	5.06 ± 0.53	5.60 ± 0.19	4.29 ± 0.45	4.21 ± 0.75	4.40 ± 0.22
Lungs	1.47 ± 0.05	1.52 ± 0.20	1.76 ± 0.06	1.67 ± 0.07	1.81 ± 0.04	1.58 ± 0.07	1.82 ± 0.10
Kidney	1.35 ± 0.08	1.17 ± 0.18	1.23 ± 0.10	1.52 ± 0.12	1.72 ± 0.05	1.79 ± 0.17	1.42 ± 0.15
Stomach	1.45 ± 0.15	1.01 ± 0.04	1.40 ± 0.23	1.39 ± 0.11	1.68 ± 0.08	1.96 ± 0.33	2.17 ± 0.20
Heart	0.99 ± 0.30	0.58 ± 0.08	0.64 ± 0.04	0.63 ± 0.06	0.65 ± 0.07	0.65 ± 0.04	0.79 ± 0.10
Spleen	0.67 ± 0.01	0.68 ± 0.06	0.66 ± 0.06	0.70 ± 0.04	0.67 ± 0.04	0.96 ± 0.08	1.31 ± 0.18
Testes	2.33 ± 0.15	1.77 ± 0.40	2.29 ± 0.07	2.44 ± 0.07	2.22 ± 0.04	2.11 ± 0.40	2.52 ± 0.26
Female							
Liver	4.23 ± 0.26	4.88 ± 0.45	4.07 ± 041	5.14 ± 0.14	3.79 ± 0.08	3.72 ± 0.11	3.91 ± 0.11
Lungs	1.24 ± 0.10	1.55 ± 0.23	1.47 ± 0.29	1.38 ± 0.14	1.63 ± 0.08	1.75 ± 0.16	1.75 ± 0.16
Kidney	1.09 ± 0.06	0.92 ± 0.06	0.94 ± 0.09	0.78 ± 0.03	1.51 ± 0.04	1.64 ± 0.04	1.64 ± 0.04

Stomach	1.13 ± 0.06	0.96 ± 0.11	0.92 ± 0.11	1.24 ± 0.05	1.64 ± 0.16	1.53 ± 0.18	1.97 ± 0.12
Heart	0.58 ± 0.01	0.52 ± 0.04	0.49 ± 0.02	0.53 ± 0.03	0.52 ± 0.04	0.59 ± 0.03	0.62 ± 0.03
Spleen	0.60 ± 0.04	0.75 ± 0.08	0.51 ± 0.02	0.60 ± 0.03	0.74 ± 0.02	0.70 ± 0.05	0.78 ± 0.34
Uterus	0.47 ± 0.01	0.45 ± 0.11	0.44 ± 0.12	0.44 ± 0.03	0.30 ± 0.05	0.63 ± 0.01	0.62 ± 0.05

Values are expressed as mean ± SEM (n=5)

Table 10: Effect of treatment on haematological parameters on male rats.

Parameters		100 mg		250 mg		500 mg	
	Normal	HSE	MSE	HSE	MSE	HSE	MSE
Male							
WBCx10^3/µL	10.13 ± 1.65	12.87 ± 3.34	16.14 ± 0.73[a]	12.03 ± 1.52	17.03 ± 0.52[a]	19.57 ± 1.21[a]	25.55 ± 0.16[a]
RBCx10^6/µL	8.37 ± 0.51	8.95 ± 0.70	8.64 ± 0.53	9.97 ± 0.37	7.89 ± 0.49	7.51 ± 0.91	8.03 ± 0.21
HGB g/dL	14.00 ± 0.96	15.10 ± 0.35	14.36 ± 0.94	15.81 ± 3.20	14.41 ± 0.76	16.63 ± 3.06	14.57 ± 0.64
HCT%	48.73 ± 3.84	53.40 ± 1.47	50.91 ± 1.00	50.90 ± 3.59	50.57 ± 2.01	47.98 ± 2.79	51.80 ± 1.10
MCV fL	58.07 ± 1.09	61.00 ± 3.63	63.00 ± 2.53	54.93 ± 1.64	64.20 ± 1.36	55.87 ± 3.20	64.53 ± 1.65
MCH pg	16.70 ±0.12	17.27 ± 1.12	17.77 ± 0.77	16.93 ± 1.64	16.50 ± 0.60	15.73 ± 0.76	18.17 ± 0.72
LYM%	86.67 ± 2.23	82.20 ± 1.72	80.13 ± 0.95	83.93 ± 2.98	80.65 ± 2.68	79.10 ± 1.87	83.05 ± 2.10
NEUT%	19.33 ± 2.23	18.87 ± 0.58	19.87 ± 0.95	21.07 ± 2.98	18.27 ± 1.89	21.60 ± 1.84	19.56 ± 1.80
RDW-SD fL	39.53 ± 1.27	38.37 ± 3.28	40.20 ± 4.47	38.47 ± 1.16	40.28 ± 1.79	38.60 ± 0.96	42.43 ± 2.09
RDW-CV %	16.47 ± 0.58	16.83 ± 0.69	17.27 ± 1.42	16.97 ± 0.95	18.57 ± 1.33	17.63 ± 0.70	18.10 ± 0.40
PDW fL	11.70 ± 0.70	8.23 ± 0.33	9.97 ± 1.05	8.37 ± 0.22	9.70 ± 0.29	8.97 ± 0.78	11.83 ± 1.40
MPV fL	8.33 ± 0.12	7.87 ± 0.12	7.80 ± 0.50	7.93 ± 0.23	7.70 ± 0.10	7.87 ± 0.43	8.67 ± 0.48
P-LCR %	16.23 ± 1.23	15.53 ± 0.72	14.82 ± 0.96	15.53 ± 1.01	15.81 ± 1.07	16.47 ± 2.58	17.30 ± 4.17
PCT %	0.85 ± 0.08	0.55 ± 0.04	0.43 ± 0.09	0.70 ± 0.10	0.50 ± 0.05	0.43 ± 0.09	0.61 ± 0.18
PLT (uL)	842.67 ± 80.42	897.00 ± 75.12	784.67 ± 14.52	880.33 ± 63.28	922.33 ± 49.33	952.00 ± 30.24	819.67 ± 79.71

Values are expressed as mean ±SEM (n=5). Superscript "a" is significant at P<0.05-0.01 compared with the normal group.

Table 11: Effect of treatment on haematological parameters on Female rats.

Parameters		100 mg		250 mg		500 mg	
	Normal	HSE	MSE	HSE	MSE	HSE	MSE
Female							
WBCx10^3/µL	11.53 ± 0.58	12.50 ± 2.00	15.98 ± 0.90[a]	15.85 ± 0.71[a]	21.33 ± 0.62[a]	11.07 ± 1.29	17.13 ± 1.90[a]
RBCx10^6/µL	8.64 ± 0.06	7.86 ± 0.68	7.41 ± 0.39	8.64 ± 0.54	8.27 ± 0.63	7.93 ± 0.49	9.24 ± 0.58
HGB g/dL	15.20 ± 0.12	14.87 ± 1.28	14.50 ± 1.80	14.47 ± 0.54	13.27 ± 0.62	14.23 ± 0.47	13.07 ± 0.58
HCT%	50.30 ± 0.17	42.33 ± 4.35	50.53 ± 2.45	51.33 ± 0.32	51.47 ± 0.31	48.87 ± 2.43	48.64 ± 1.05
MCV fL	58.20 ± 0.46	61.73 ± 1.62	64.20 ± 0.81	59.90 ± 3.45	64.00 ± 0.31	61.73 ± 1.82	60.27 ± 1.45
MCH pg	17.60 ± 0.06	18.77 ± 0.60	19.03 ± 0.27	17.67 ± 1.41	17.70 ± 1.62	18.47 ± 0.58	19.43 ± 0.43
LYM%	82.70 ± 3.98	75.13 ± 4.68	87.80 ± 1.48	77.23 ± 2.50	79.50 ± 2.24	76.03 ± 6.87	78.57 ± 1.66
NEUT%	19.30 ± 3.98	22.87 ± 4.68	18.19 ± 1.27	22.77 ± 2.50	20.50 ± 2.24	20.97 ± 6.87	21.43 ± 1.66
RDW-SD fL	36.77 ± 2.42	29.57 ± 0.66	42.83 ± 2.14	29.53 ± 0.72	40.90 ± 1.14	30.43 ± 2.24	42.63 ± 2.68
RDW-CV %	12.63 ± 1.31	11.67 ± 0.61	12.13 ± 0.82	11.83 ± 0.69	13.00 ± 1.00	12.10 ± 1.17	11.13 ± 2.49
PDW fL	11.77 ± 0.77	9.77 ± 0.38	10.03 ± 0.34	11.57 ± 0.13	10.50 ± 0.10	10.00 ± 0.36	10.57 ± 0.13
MPV fL	8.07 ± 0.03	7.37 ± 0.29	7.57 ± 0.18	7.27 ± 0.12	8.33 ± 0.09	7.83 ± 0.26	8.30 ± 0.25
P-LCR %	13.97 ± 0.26	11.27 ± 1.68	12.40 ± 1.27	10.93 ± 0.83	13.80 ± 0.40	11.53 ± 1.09	14.27 ± 1.23
PCT %	0.53 ± 0.03	0.52 ± 0.13	0.52 ± 0.09	0.77 ± 0.04	0.54 ± 0.03	0.72 ± 0.05	0.53 ± 0.05
PLT (uL)	781.33 ± 36.54	714.33 ± 98.14	778.73 ± 41.84	859 ± 63.26	843.67 ± 30.39	853.67 ± 40.99	738.67 ± 38.35

Values are expressed as mean ±SEM (n=5). Superscript "a" significant at P<0.05-0.01 compared with the normal group

Table 12: Effect of Treatment on Non-Invasive Inflammatory Indices.

	Male			Female		
Treatment	**PLR**	**NLR**	**PLR+NLR**	**PLR**	**NLR**	**PLR+NLR**
Normal	89.80 ± 36.70	0.27 ± 0.04	90.07 ± 36.67	76.45 ± 7.79	0.22 ± 0.06	76.67 ± 7.82
100 mg HSE	92.51 ± 8.10	0.22 ± 0.03	92.73 ± 8.11	73.44 ± 14.57	0.34 ± 0.09	73.78 ± 14.49
250 mg HSE	90.98 ± 38.71	0.36 ± 0.05	91.34 ± 38.76	72.90 ± 7.35	0.30 ± 0.04	73.20 ± 7.38
500 mg HSE	93.64 ± 37.94	0.27 ± 0.03	93.91 ± 37.97	74.34 ± 37.03	0.26 ± 0.13	74.60 ± 37.13
100 mg MSE	85.56 ± 18.53	0.25 ± 0.01	85.81 ± 18.54	78.46 ± 5.50	0.14 ± 0.02	78.60 ± 5.49
250 mg MSE	90.04 ± 10.35	0.26 ± 0.06	90.30 ± 10.38	81.51 ± 5.73	0.26 ± 0.04	81.77 ± 5.76
500 mg MSE	90.32 ± 12.27	0.24 ± 0.19	90.56 ± 12.22	77.07 ± 2.40	0.27 ± 0.03	77.34 ± 2.37

Values are expressed as mean ± SEM (n=5). PLR, Platelet Lymphocyte Ratio; NLR, Neutrophil Lymphocyte Ratio

Table 13: Effect of treatment on biochemical parameters in male rats.

Parameters		100 mg		250 mg		500 mg	
	Normal	HSE	MSE	HSE	MSE	HSE	MSE
Male							
AST (U/L)	125.37 ± 7.21	119.00 ± 10.02	122.00 ± 3.06	116.27 ± 12.71	121.00 ± 2.89	115.73 ± 2.41	133.00 ± 7.20
ALT (U/L)	42.67 ± 1.45	42.00 ± 4.04	39.00 ± 3.61	48.33 ± 0.86	41.80 ± 5.14	46.04 ± 1.08	44.83 ± 2.92
CKMB (U/L)	1569.21 ± 342.26	1616.00 ± 88.64	1595.5 ± 135.54	1599.9 ± 42.54	1475.8 ± 236.88	1741.6 ± 35.52	1695.5 ± 67.53
LDH (U/L)	4059.2 ± 170.42	3863.3 ± 140.71	4006.0 ± 213.51	3991.5 ± 110.13	4235.9 ± 176.62	4152.4 ± 93.38	3928.4 ± 96.70
Creatinine (mmol/L)	39.77 ± 1.61	36.07 ± 0.87	37.50 ± 3.43	39.50 ± 6.16	44.34 ± 3.69	39.65 ± 1.11	47.08 ± 3.42
Urea (mmol/L)	7.37 ± 0.18	8.42 ± 0.49	7.31 ± 1.02	8.33 ± 0.59	10.63 ± 1.54	9.06 ± 0.53	12.22 ± 2.54
TCHOL. (mmol/l)	1.90 ± 003	1.90 ± 0.80	1.56 ± 0.36	2.07 ± 0.14	1.83 ± 0.25	2.12 ± 0.11	2.46 ± 0.05
TRIG. (mmol/l)	0.64 ± 0.05	0.78 ± 0.15	0.62 ± 0.15	0.87 ± 0.08	0.72 ± 0.02	0.93 ± 0.05	0.85 ± 0.07
HDL-C (mmol/l)	0.91 ± 002	0.90 ± 0.15	1.25 ± 0.25	0.93 ± 0.19	1.16 ± 0.16	0.97 ± 0.12	1.11 ± 0.37
LDL-C (mmol/l)	0.86 ± 0.02	0.90 ± 0.06	1.08 ± 0.22	1.17 ± 0.20	1.15 ± 0.36	1.10 ± 0.23	1.19 ± 0.15
VLDL (mmol/l)	0.39 ± 0.02	0.33 ± 0.09	0.39 ± 0.06	0.35 ± 0.04	0.47 ± 0.16	0.38 ± 0.02	0.42 ± 0.13
Potassium (mmol/L)	8.13 ± 0.31	8.58 ± 0.80	11.58 ± 2.06	10.81 ± 0.77	9.98 ± 1.78	10.08 ± 1.47	13.72 ± 1.07
Sodium (mmol/L)	143.87 ± 0.64	147.21 ± 3.64	140.27 ± 9.13	139.75 ± 5.06	142.63 ± 8.59	142.20 ± 2.62	147.63 ± 8.29
Chloride (mmol/L)	103.23 ± 0.67	103.47 ± 4.22	102.63 ± 4.68	116.89 ± 1.73	114.93 ± 3.54	108.25 ± 4.57	120.60 ± 6.41

Values are expressed as mean ± SEM (n=5).

Table 14: Effect of treatment on biochemical parameters in female rats.

Parameters		100 mg		250 mg		500 mg	
	Normal	HSE	MSE	HSE	MSE	HSE	MSE
Female							
AST (U/L)	120.13 ± 5.68	131.33 ± 10.84	125.30 ± 10.84	116.33 ± 4.26	124.33 ± 4.33	122.17 ± 12.33	128.30 ± 8.66
ALT (U/L)	30.7 ± 4.19	28.33 ± 2.91	29.83 ± 0.52	30.67 ± 4.33	33.37 ± 1.41	30.67 ± 3.70	33.77 ± 2.61
CKMB (U/L)	1720.3 ± 526.82	1678.3 ± 132.20	1633.7 ± 76.72	1755.1 ± 145.11	1704.7 ± 31.42	1795.36 ± 94.8	1782.63 ± 64.83
LDH (U/L)	3968.1 ± 392.16	4002.8 ± 214.17	3646.0 ± 64.60	3886.2 ± 247.38	3912.0 ± 158.13	4112.3 ± 187.20	4126.70 ± 128.03
Creatinine (mmol/L)	46.40 ± 2.43	36.33 ± 4.91	43.67 ± 3.06	42.50 ± 4.13	48.27 ± 4.10	47.77 ± 2.23	43.43 ± 2.71
Urea (mmol/L)	9.94 ± 0.27	10.21 ± 1.92	8.78 ± 1.66	7.16 ± 1.91	8.89 ± 0.82	8.77 ± 0.78	9.70 ± 1.40
TCHOL. (mmol/l)	2.21 ± 0.16	2.79 ± 0.33	2.33 ± 0.59	3.44 ± 0.30	2.34 ± 0.40	3.69 ± 1.02	3.82 ± 0.18
TRIG. (mmol/l)	0.83 ± 0.02	0.46 ± 0.80	0.99 ± 0.26	0.76 ± 0.65	0.82 ± 0.21	0.98 ± 0.18	1.42 ± 0.10
HDL-C (mmol/l)	1.31 ± 0.11	1.39 ± 0.80	1.29 ± 0.16	1.46 ± 0.65	1.52 ± 0.15	1.52 ± 0.42	1.32 ± 0.10
LDL-C (mmol/l)	0.93 ± 0.06	0.84 ± 0.75	0.70 ± 0.08	0.90 ± 0.51	1.18 ± 0.16	1.23 ± 0.61	1.30 ± 0.10
VLDL (mmol/l)	0.38 ± 0.01	0.49 ± 0.24	0.41 ± 0.10	0.35 ± 0.47	0.49 ± 0.09	0.51 ± 0.57	0.64 ± 0.05
Potassium (mmol/L)	6.86 ± 0.48	6.33 ± 0.12	6.06 ± 0.65	6.72 ± 0.37	7.09 ± 0.57	7.11 ± 0.28	6.98 ± 1.22
Sodium (mmol/L)	144.03 ± 0.67	148.99 ± 0.74	140.00 ± 6.93	133.67 ± 0.63	150.00 ± 6.93	147.47 ± 0.82	146.67 ± 6.96
Chloride (mmol/L)	102.80 ± 0.80	105.68 ± 1.10	103.67 ± 5.24	105.43 ± 1.08	108.67 ± 3.48	107.12 ± 1.00	114.00 ± 5.29

Values are expressed as mean ± SEM (n=5).

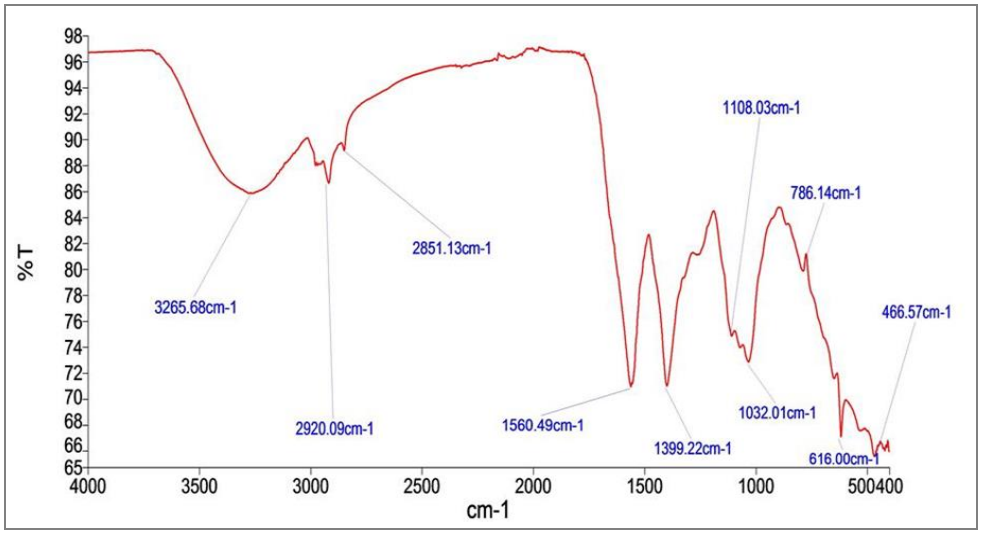


Figure 1: FTIR spectrum of *P. laxiflora* stem bark of hydroethanolic crude extract (HSE).

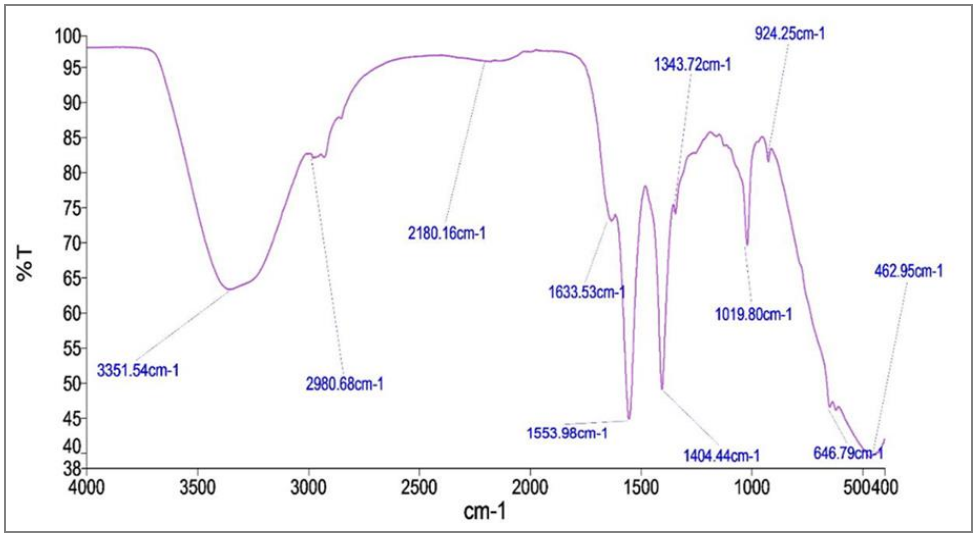


Figure 2: FTIR spectrum of *P. laxiflora* stem bark of methanolic crude extract (MSE).

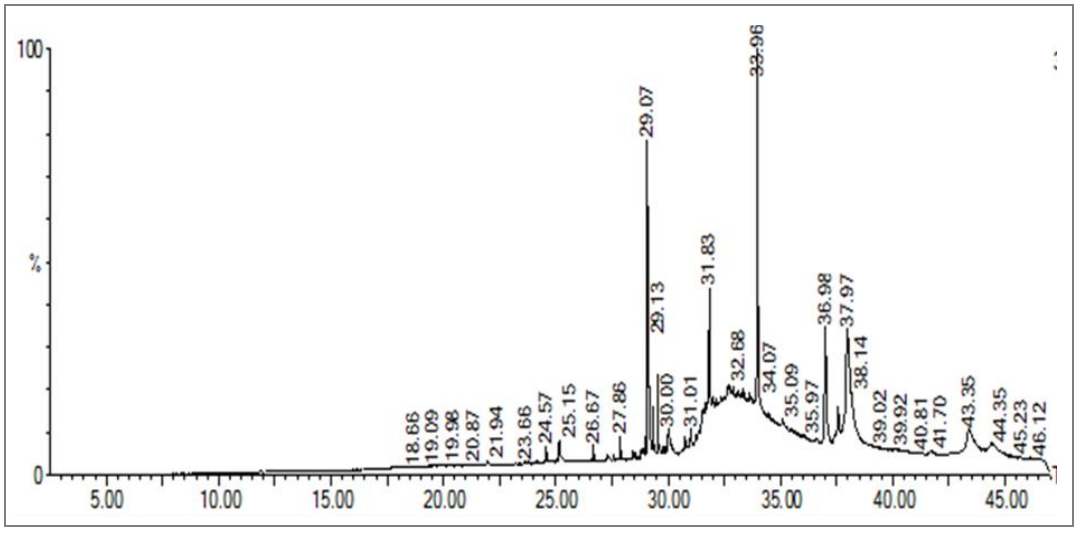


Figure 3: GC-CM spectrum showing peaks of all compounds present in HSE.

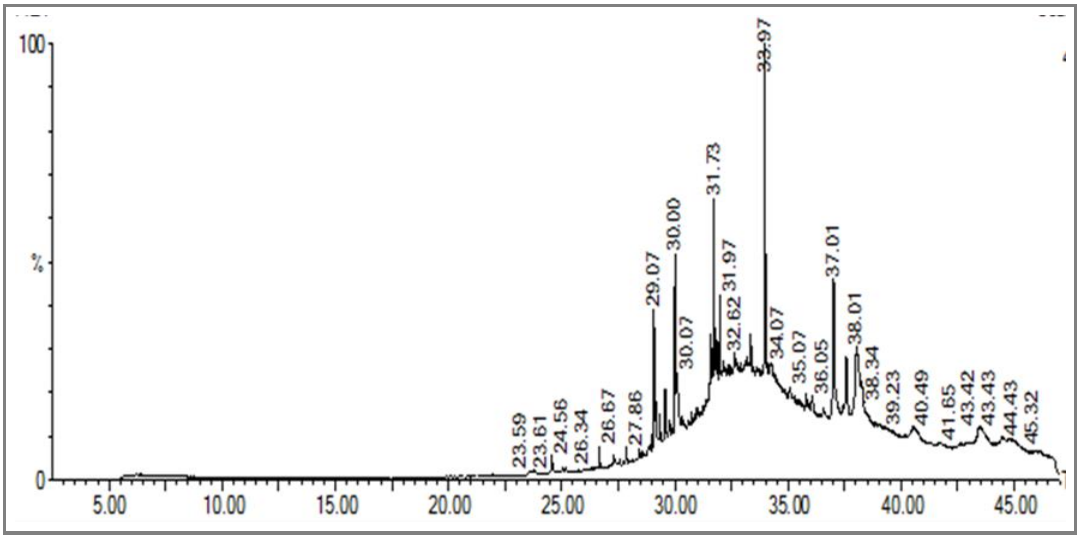


Figure 4: GC-CM spectrum showing peaks of all compounds present in MSE.

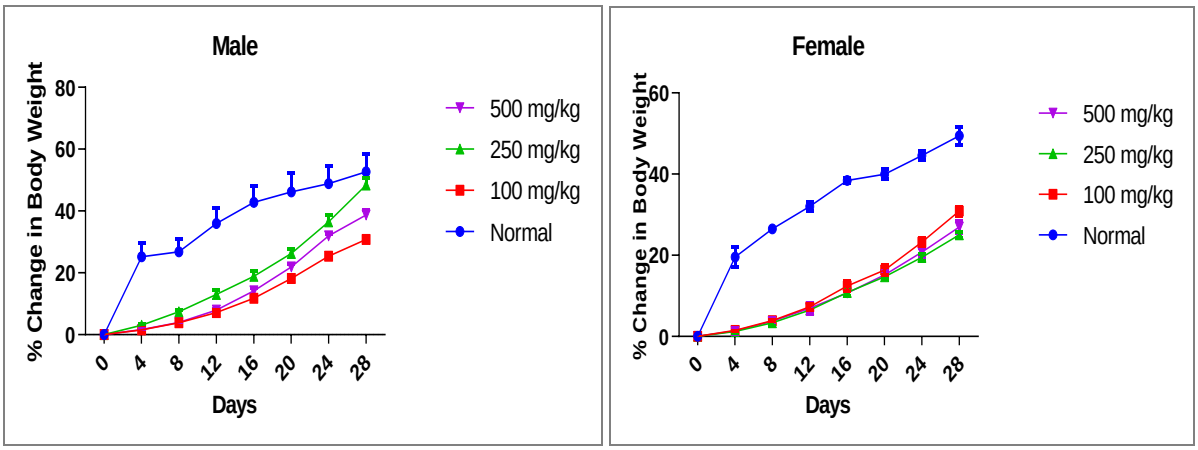


Figure 5: Effect of HSE on percent change in body weight of male and female animals. Each point represents a mean±SEM (n=5).

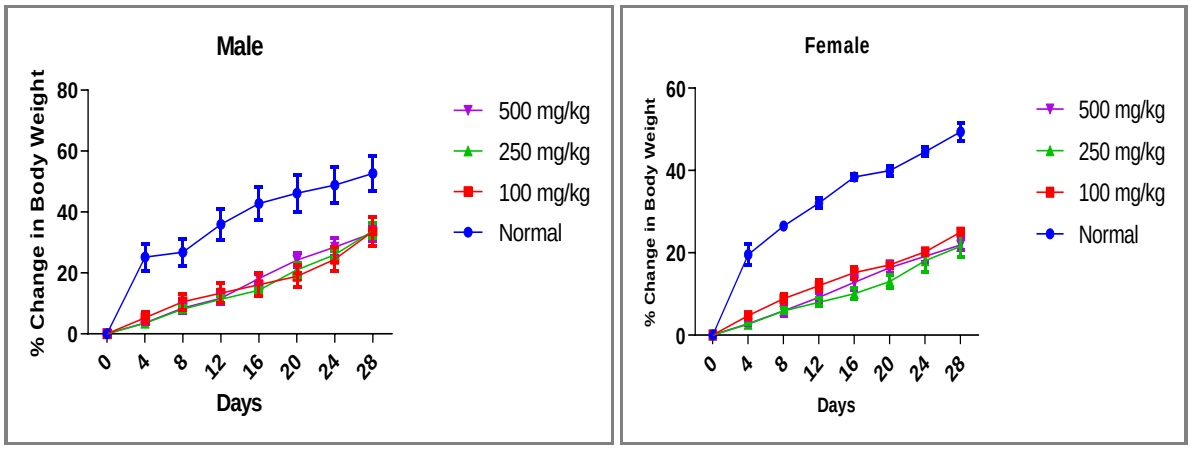


Figure 6: Effect of MSE on percent change in body weight of male and female animals. Each point represents a mean±SEM (n=5).

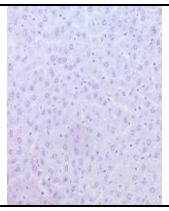
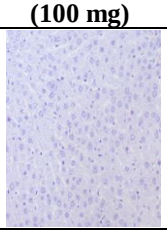
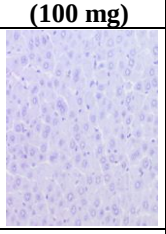
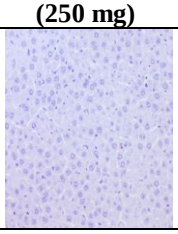
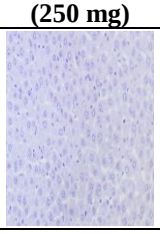
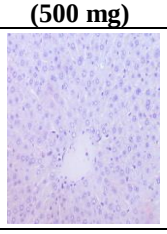
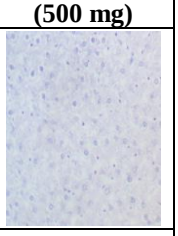
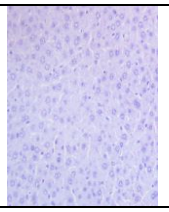
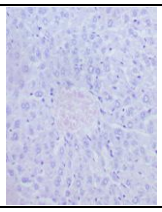
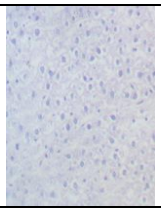
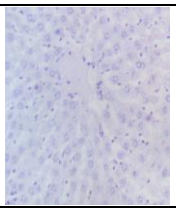
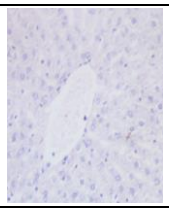
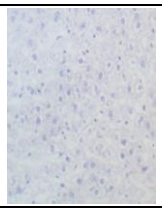
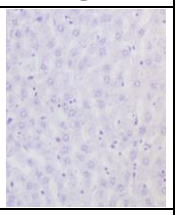
	Normal	HSE (100 mg)	MSE (100 mg)	HSE (250 mg)	MSE (250 mg)	HSE (500 mg)	MSE (500 mg)
Male							
	A	B	C	D	E	F	G
Female							
	H	I	J	K	L	M	N

Figure 7: Photomicrographs of liver from rats administered orally for 28 days with: **(A)** distilled water (control), **(B)** 100 mg/kg b.wt of HSE, **(C)** 100 mg/kg b.wt of MSE, **(D)** 250 mg/kg b.wt of HSE, **(E)** 250 mg/kg b.wt of MSE, **(F)** 500 mg/kg b.wt of HSE, **(G)** 500 mg/kg b.wt of MSE, **(H)** distilled water (control), **(I)** 100 mg/kg b.wt of HSE, **(J)** 100 mg/kg b.wt of MSE, **(K)** 250 mg/kg b.wt of HSE, **(L)** 250 mg/kg b.wt of MSE, **(M)** 500 mg/kg b.wt of HSE and **(N)** 500 mg/kg b.wt of MSE. Photomicrograph **(A) – (N)** shows normal hepatocytes with no observable lesion. (H&E X 400).

4.0 DISCUSSION

In several nations, medicinal plants and their constituents have been utilized to treat various diseases as a supplement to synthetic drug medications. Systematic research on the toxic effects of herbal plants needs to be assessed to ensure their safety by providing scientific evidence for appropriate doses for animals, including humans.[20-22] Indeed, there has been little published research on toxicity study on *Pericopsis* species including, *P. elata*[23], *P. angolensis*[24], and *P. mooniana*[25], however, no toxicological studies on either hydroethanolic or methanolic stem bark extracts of *P. laxiflora* have been conducted, although current literature has proved their medicinal purposes. Without being aware of their hazardous effects, they may be detrimental for long-term use. Therefore, the present study provides first-hand knowledge of the damaging consequences of HSE and MSE of *P. laxiflora*.

Preliminary screening of phytochemicals showed the existence of alkaloids, polyphenols, flavonoids, cyanogenic glycosides, triterpenes, tannins, saponins, reducing sugars, and phytosterol in *P. laxiflora*. Further, these compounds appear to be adequate with the antioxidant activity obtained. Indeed, many studies, including Quattara *et al.*[26], reported an excellent correlation between the presence of these compounds with their antioxidant properties. These phytochemicals, as observed in previous reports, possess pharmacological properties. In treating various disorders, tannin-rich plants are used and are known to have hypolipidemic and anti-cancer activities.[27] Flavonoids are powerful polyphenols, and their effectiveness as free radical scavengers is supported by several findings.[28-30] It is also known that alkaloids help defend against pathogens, regulating oxidative stress and hormonal action.[31] Alkaloid, flavonoid, and saponin were also recorded to be responsible for protecting the liver and kidney against carbon tetrachloride-induced toxicity in rats via preventing oxidative stress.[32] Glycosides are also reported to have anti-protozoan effects, antimicrobial properties and are also used as astringents.[33] Sodium-potassium-ATPases are inhibited by glycosides and can cause a decrease in the heart rate. The anti-inflammatory, insecticidal, sedative, and cytotoxic activities of triterpenoids are also reported.[34] A synergy of therapeutic effects is assumed to be produced by these phytochemicals.[35]

The FTIR spectra indicate the different functional groups such as phenols, alkanes, carboxylic acid aromatics, alkynes and alcohols, which could support the phytoconstituents of *P. laxiflora*. Furthermore, the GCMS spectrum predicted possible compounds such phenols, oleic acid, and phytol that could have pharmacological activities (including hepatoprotective and anti-fibrotic effects). The ability of the various extracts to stabilize free radicals was evaluated using a DPPH scavenging assay. Methanol extract had a stronger scavenging activity than HSE. The HSE was however highest in TPC, TT, and TFC values. Total phenols derived from plants are potent antioxidants with the potential for carcinogenesis inhibition.[36]

In some medicinal plants, heavy metal concentration has been confirmed, explaining some of the related toxicity.[37] With this regard, the extract was evaluated for some heavy metals. There was no detection of iron, zinc, lead, nickel, and copper in the crude extract, however, iron and zinc were recorded in low concentrations (0.009 ± 0.00; 0.004 ± 0.00, respectively) in the raw powdered sample. Toxicity testing is the sole scientific foundation for certifying the safety of plant-based medicines in traditional disease treatment. It has also been suggested that all-natural medicinal products be submitted to the same safety studies as new orthodox medicines.[38]

Lethal Dose (LD_{50}) $\geq$ 5000 mg/kg b.wt in the acute toxicity study suggests that HSE and MSE are safe for use under acute conditions. The subacute toxicity study provides data that can be used to make decisions on a secure amount of

dose target organ toxicity, and potentially harmful consequences on animal models. The effect of HSE and MSE in rats was evaluated in this study at doses of 100, 250, and 500 mg/kg b.wt. for 28 days in both sexes. One index of toxicity is weight loss in treated animals.[39] Generally, weight gains were observed in treated animals as they were fed, demonstrating that the extracts were not toxic at various doses. Weight loss is known to occur as a result of toxic material administration, altering appetite and disrupting the metabolism of carbohydrates, proteins, or fats.[39] Moreover, there were no significant differences in the relative organ weights compared to untreated animals, further suggesting that extracts were not toxic at the different doses administered.

Generally, haematological indices are valuable tools for monitoring toxicity in animals. This is important because it can alter the expected range of parameters by ingesting toxic or foreign substances.[40] The treated animals showed significant increases in white blood cell counts at higher doses of 500 mg/kg for both sexes in HSE and all doses (100, 250, and 500mg/kg) in both sexes in MSE. WBC increase is a marker of stress and a mechanism of defence against inflammatory conditions[12] and likely an adaptive response scenario. Also, the haematological parameters (Table 10 and 11) in most treated animals were non-significantly different from those of the controls, which further established that these extracts are non-toxic in animals at the studied doses. These results generally further confirm that there are no toxic effects of HSE and MSE on treated animals.

The liver plays a vital role in the metabolism of foreign compounds, fats, carbohydrates, and proteins. This, therefore, means that both the liver and the kidney are vulnerable to damage caused by drugs.[41] This has made it convenient to check the safety of the plant extracts as they relate to these two organs, along with the continuous and global increase in liver and kidney diseases particularly with drug-induced liver injury (DILI). Compared to the control, there were no significant differences in all biochemical parameters. To evaluate liver injury, ALT is a better parameter, and the absence of significant changes at all doses suggests that the extract may not be toxic to the liver. High creatinine and urea levels in the blood suggest renal failure, whereas low creatinine and urea levels indicate appropriate kidney function.[42] The safety of the extracts is suggested by non-significant differences in creatinine and urea levels in the treated animals and controls. The non-significant differences in electrolyte levels are also a strong indicator of the probable non-deleterious effects of treatments on the kidneys. Compared to controls, a non-significant difference in triglycerides and cholesterol concentration indicated that the metabolisms of carbohydrates and lipids have not been disturbed, which further confirms the safety of plant extract orally.

LDH is released in tumour situations because of several cytokine activities and cell membrane damage.[31] In the present study, there were no elevated cases of LDH and CKMB, thus ruling out unusual proliferation and damage to cells such as cardiovascular cells, red blood cells, and hepatocytes in treated animals.

Another means of safety testing for drug-induced toxicity is the histopathological examination of tissue, especially the liver post-treatment.[43] No major pathological alteration was observed in the gross and histopathological examination of the liver.

CONCLUSION

The present study on hydroethanolic and methanolic stem bark extract of *P. laxiflora* shows that it has phytoconstituents that have therapeutic effects. It was estimated that the LD_{50} was above 5000 mg/kg b.wt indicating safety. Based on the biochemical parameters of this study, HSE and MSE are safe at orally administered doses.

Histopathological examination of the liver showed no visible lesion after treatment with extracts at all doses. However, increases in WBCs in both the male and female rats may be an adaptive response for the rats. This study proves the safety and antioxidant properties of the *Pericopsis laxiflora* extract hence the need to further explore the pharmacological activities for commercial exploitation.

Data Availability

The data used to support the findings of this study are available within the article.

Acknowledgment

The authors are grateful to the University for Development Studies for providing the laboratory to support this study.

Authorship Contribution Statement

Frederick Sarfo-Antwi: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. Christopher Larbie: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. Benjamin Obukowho Emikpe: Conceptualization, Methodology, Formal analysis, Investigation. Regina Appiah–Opong and Daniel Seifu: Conceptualization, Methodology, Formal analysis, Investigation.

Funding

No funding was received for this work.

Disclosure

The authors report no conflicts of interest for this work.

REFERENCES

1. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: History and future perspective. *Journal of HerbMed Pharmacology*, 2018; 7(1): 1-7.
2. Vadhana P, Singh BR, Bharadwaj M, Singh SV. The emergence of herbal antimicrobial drug resistance in clinical bacterial isolates. *Pharm Anal Acta*, 2015; 6(10): 434.
3. Nasri H. Toxicity and safety of medicinal plants. *Journal of HerbMed Pharmacology*, 2013; 2(1): 15.
4. Goncalves J, Rosado T, Soares S, Simão AY, Caramelo D, Luís A, Duarte AP. Cannabis and its secondary metabolites: Their use as therapeutic drugs, toxicological aspects, and analytical determination. *Medicines*, 2019; 6(1): 31.
5. Aina O, Gautam L, Simkhada P, Hall S. Prevalence, determinants, and knowledge about herbal medicine and non-hospital utilization in southwest Nigeria: A cross-sectional study. *BMJ Open*, 2020; 10(9): e040769.
6. Sen S, Chakraborty R. Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: Importance, challenges, and future. *Journal of Traditional and Complementary Medicine*, 2017; 7(2): 234-244.
7. Imoro AZ, Aikins TK, Eledi JDA. Exploitation and use of medicinal plants, Northern Region, Ghana, 2013.
8. Ayoola GA, Coker HA, Adesegun SA, Adepoju-Bello AA, Obaweya K, Ezennia EC, Atangbayila TO. Phytochemical screening and antioxidant activities of some selected medicinal plants used for malaria therapy in Southwestern Nigeria. *Tropical Journal of Pharmaceutical Research*, 2008; 7(3): 1019-1024.

9. Povolo C, Foschini A, Ribaudo G. Optimization of the extraction of bioactive molecules from *Lycium barbarum* fruits and evaluation of the antioxidant activity: a combined study. *Natural Product Research*, 2019; 33(18): 2694-2698.
10. Zhang H, Yang YF, Zhou ZQ. Phenolic and flavonoid contents of mandarin (*Citrus reticulata* Blanco) fruit tissues and their antioxidant capacity as evaluated by DPPH and ABTS methods. *Journal of Integrative Agriculture*, 2018; 17(1): 256-263.
11. Naz R, Roberts TH, Bano A, Nosheen A, Yasmin H, Hassan MN, Anwar Z. GC-MS analysis, antimicrobial, antioxidant, antilipoxygenase, and cytotoxic activities of *Jacaranda mimosifolia* methanol leaf extracts and fractions. *PloS One*, 2020; 15(7): e0236319.
12. Karbiner MS, Sierra L, Minahk C, Fonio MC, de Bruno MP, Jerez S. The role of oxidative stress in alterations of hematological parameters and inflammatory markers induced by early hypercholesterolemia. *Life Sciences*, 2013; 93(15): 503-508.
13. Maheshwaran MV, Hyness NRJ, Senthamaraikannan P, Saravanakumar SS, Sanjay MR. Characterization of natural cellulosic fiber from *Epipremnum aureum* stem. *Journal of Natural Fibers*, 2018; 15(6): 789-798.
14. Larbie C, Mills-Robertson FC, Quaicoe EB, Opoku R, Kabiri NC, Abrokwah RO. *Tetrapleura tetraptera* of Ghanaian Origin: Phytochemistry, Antioxidant and Antimicrobial Activity of Extracts of Plant Parts. *Journal of Pharmaceutical Research International*, 2020; 32(35): 78-96.
15. Zoufan P, Jalali R, Karimiafshar A, Motamedi H. Assessment of heavy metal accumulation and antibacterial activity of some medicinal herbs grown in an industrial area of steel production, Ahvaz. *Iranian Journal of Pharmaceutical Sciences*, 2017; 13(1): 73-78.
16. National Research Council. Environment, housing, and management. In: *Guide for Care and Use of Laboratory Animals*, 2011; 8: 43-45.
17. Organisation for Economic Co-operation and Development. OECD Acute oral toxicity: up and down procedure. *Guideline for the Testing of Chemicals*, 2008; 425: 1-2.
18. Arthur FKN, Woode E, Terlabi EO, Larbie C. Evaluation of acute and subchronic toxicity of *Annona muricata* (Linn.) aqueous extract in animals. *European Journal of Experimental Biology*, 2011; 1(4): 115-124.
19. Organisation for Economic Co-operation and Development. Test No. 407: Repeated Dose 28-day Oral Toxicity Study in Rodents. *OECD Guidelines for the Testing of Chemicals*, 2008; 4.
20. Calixto JB. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). *Brazilian Journal of Medical and Biological Research*, 2000; 33(2): 179-189.
21. Saad, B., Zaid, H., Shanak, S., and Kadan, S. Introduction to medicinal plant safety and efficacy. In *Anti-diabetes and anti-obesity medicinal plants and phytochemicals* (pp. 21-55). Springer, Cham, 2017.
22. Chen, H., Diao, X., Wang, H., and Zhou, H. An integrated metabolomic and proteomic study of toxic effects of Benzo [a] pyrene on gills of the pearl oyster *Pinctada martensii*. *Ecotoxicology and Environmental Safety*, 2018; 156: 330-336.
23. Ajaiyeoba, E. O., Abiodun, O. O., Falade, M. O., Ogbole, N. O., Ashidi, J. S., Happi, C. T., and Akinboye, D. O. In vitro cytotoxicity studies of, 20 plants used in Nigerian antimalarial ethnomedicine. *Phytomedicine*, 2006; 13(4): 295-298.

24. Gracia, A. A., Valentin, B. C., Henry, M. M., Arlette, K. M., and Salvius, B. A. In vitro antioxidant activity and in vivo aphrodisiac activity in male *Cavia porcellus* of *Albizia adianthifolia* (Schum.) W. Wight and *Pericopsis angolensis* (Baker) Meeuwen. *World Journal of Biology Pharmacy and Health Sciences*, 2021; 5(3): 044-052.
25. Yudohartono, T. P., and Fiani, A. Genetic diversity of kayu kuk u (*Pericopsis mooniana* Thw) from southeast Sulawesi provenance observed at seedling stage. *Journal Pemuliaan Tanaman Hutan*, 2019; 13(1): 11-17.
26. Quattara, A., Kouame, A., Tiebre, M. S., Cisse, A., and N'guessan, K. Flora diversity and plant use in the Sudanese zone of northwestern Côte d'Ivoire. *Journal of Animal and Plant Sciences*, 2016; 31: 4828-4840.
27. Yao, J. C., Hassan, M., Phan, A., Dagohoy, C., Leary, C., Mares, J. E., and Evans, D. B. One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *Journal of Clinical Oncology*, 2008; 26(18): 3063-3072.
28. Amic, A., Lučić, B., Stepanić, V., Marković, Z., Marković, S., Marković, J. M. D., and Amić, D. Free radical scavenging potency of quercetin catecholic colonic metabolites: Thermodynamics of 2H+/2e− processes. *Food Chemistry*, 2017; 218: 144-151.
29. Es-Safi, N. E., Ghidouche, S., and Ducrot, P. H. Flavonoids: hemisynthesis, reactivity, characterization, and free radical scavenging activity. *Molecules*, 2007; 12(9): 2228-2258.
30. Kaurinovic, B., and Vastag, D. Flavonoids and phenolic acids as potential natural antioxidants. In *Antioxidants* (pp. 1-20). London, UK: IntechOpen, 2019.
31. Jurisic, V., Radenkovic, S., and Konjevic, G. The actual role of LDH as a tumor marker, biochemical and clinical aspects. In *Advances in Cancer Biomarkers* (pp. 115-124). Dordrecht: Springer, 2015.
32. Sarfo-Antwi, F., Larbie, C., and Babatunde, D. Extracts of *Ageratum conyzoides* L. Protects against carbon tetrachloride-induced toxicity in rats through inhibiting oxidative stress. *Journal of Advances in Medical and Pharmaceutical Sciences*, 2018; 19(2): 1-14.
33. Upadhyay, R. K., and Ahmad, S. Ethno-medicinal plants and their pharmaceutical potential. *Journal of Pharmaceutical Sciences*, 2012; 5(4): 2162-2173.
34. Liu, R. H. Potential synergy of phytochemicals in cancer prevention: mechanism of action. *The Journal of Nutrition*, 2004; 134(12): 3479S-3485S.
35. Mensah, J. K., and Amarh, M. A. Antioxidant, antimicrobial, and anti-inflammation activities of *Telfairia occidentalis* seeds extract. *Current Science Perspectives*, 2019; 5: 14-23.
36. Witaicenis, A., Roldão, E. F., Seito, L. N., Rocha, N. P., and Di Stasi, L. C. Pharmacological and toxicological studies of *Drimys angustifolia* Miers (Winteraceae). *Journal of Ethnopharmacology*, 2007; 111(3): 541-546.
37. Saleh, H. M., Aglan, R. F., and Mahmoud, H. H. *Ludwigia stolonifera* for remediation of toxic metals from simulated wastewater. *Chemistry and Ecology*, 2019; 35(2): 164-178.
38. Krause, J., and Tobin, G. Discovery, development, and regulation of natural products. In *Using old solutions to new problems-natural drug discovery in the 21st century* (pp. 1-35), 2013.
39. Rajeh, M. A. B., Kwan, Y. P., Zakaria, Z., Latha, L. Y., Jothy, S. L., and Sasidharan, S. Acute toxicity impacts of *Euphorbia hirta* L extract on behavior, organs body weight index and histopathology of organs of the mice and *Artemia salina*. *Pharmacognosy Research*, 2012; 4(3): 170.
40. David, M., Sangeetha, J., Shrinivas, J., Harish, E. R., and Naik, V. R. Effects of deltamethrin on hematological indices of Indian major carp, *Cirrhinus mrigala* (Hamilton). *International Journal of Pure and Applied Zoology*, 2015; 3(1): 37-43.

41. Al-Hashem, F. Camel's milk protects against aluminum chloride-induced toxicity in the liver and kidney of white albino rats. *American Journal of Biochemistry and Biotechnology*, 2009; 5(3): 98-109.
42. Pandya, D., Nagrajappa, A. K., and Ravi, K. S. Assessment and correlation of urea and creatinine levels in saliva and serum of patients with chronic kidney disease, diabetes, and hypertension–a research study. *Journal of Clinical and Diagnostic Research*, 2016; 10(10): ZC58.
43. Prabu, P. C., Panchapakesan, S., and Raj, C. D. Acute and sub-acute oral toxicity assessment of the hydroalcoholic extract of *Withania somnifera* roots in Wistar rats. *Phytotherapy Research*, 2013; 27(8): 1169-1178.