Journal of Research in Applied and Basic Medical Sciences

ORIGINAL RESEARCH ARTICLE

Toxicological and Histopathological Screening of Some Medicinal Plant Extracts Used as Protectants Against Insect Infestation

Tejumade Mary Philip-Attah[1], Olumuyiwa Temitope Omotoso[1], Margaret Olutayo Alese[2], Olusola Michael Obembe[3]

Published: 15 August 2025

Abstract

Background The use of medicinal plants as alternatives to synthetic chemicals in combating stored product pests is gaining more attention. Plants are known for their medicinal and insecticidal properties; however, the safety of these plants for humans needs further investigation. The toxicities of ethanol extracts of *Uvaria chamae* root bark, *Mallotus oppositifolius* leaf, *Tabernaemontana pachysiphon leaf*, *Jatropha multifida* stem bark, and *Anthocleista djalonensis* stem bark were studied in BALB/c mice.

Methods Healthy female mice were randomly divided into 11 groups with three mice in each group (n = 3). The extracts were administered to the experimental mice at dosages of 300 mg/kg and 2000 mg/kg only. The control group received the vehicle orally, while the test groups were administered either 300 mg/kg or 2000 mg/kg of the extracts as single doses for 14 days. Under ether anaesthesia, blood samples were collected for liver and kidney function tests, while liver and kidney biopsies were prepared for pathological screening using the H & E technique.

Results Organs of test animals subjected to gross necropsy examination were devoid of gross pathology. The mice's body weights remained consistent throughout the experiment, indicating no significant increase ($p > 0.05$) as the actual weight change was minimal relative to the control group. At 300 and 2000 mg/kg, a regular histoarchitecture of the renal tissues was observed across all study groups relative to the control group. The actual numerical trend for the biochemical parameters, including aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total protein, urea, and creatinine, remained within the normal range of mouse biochemistry and did not differ significantly ($p > 0.05$) across all groups.

Conclusion This study thus provided some preliminary justifications for using the plants at the tested dose levels (not above 2000 mg/kg of treatment), recommending them as safe for use as stored product protectants.

Keywords Acute toxicity, *Anthocleista djalonensis*, BALB/c mice, Histopathology, *Tabernaemontana pachysiphon*, *Uvaria chamae*

✉ Tejumade Mary Philip-Attah
tejumadephilipattah@gmail.com

1. Department of Zoology and Environmental Biology, Ekiti State University, Ado-Ekiti, Nigeria
2. Department of Anatomy, College of Medicine, Ekiti State University, Ado-Ekiti, Nigeria
3. Department of Plant Science and Biotechnology, Ekiti State University, Ado-Ekiti, Nigeria

Received: 17 February 2025/ Revised: 09 April 2025/ Accepted: 09 April 2025

1 Introduction

A medicinal plant is any plant which, in one or more of its parts, contains substances that can be used for therapeutic purposes or which are precursors for the synthesis of useful drugs.[1] Humans have been using medicinal plants since time immemorial for the treatment of various ailments, often without full knowledge of their toxicity. According to,[2] the World Health Organization (WHO) estimates that about 70 to 80% of the population in developing countries use traditional medicine as a major source of health care. Aside from medicinal uses, several post-harvest researchers have also found plants useful in combating pest infestation in both field and stored products.[3-8]

Anthocleista species are shrub-like plants with heights typically ranging from 6-20 m. Formerly classified under the family Loganiaceae, they now belong to the Gentianaceae family within the major group Angiosperms.[9] The genus contains 14 species distributed across tropical Africa, Madagascar, and the Comoros, among which *A. djalonensis* A. Chev. is found.[9-11] They are generally called "Cabbage trees" in the English language,[12] with other indigenous names in Nigeria. [13, 14] The traditional medicinal uses of *A. djalonensis* include the treatment of gastrointestinal discomfort, fever, constipation, inflammatory diseases, diabetes, and wounds.[15,16] Ethno-medicinally, it is mostly used for the treatment of constipation, malaria fever, typhoid fever, hypertension, haemorrhoids, syphilis, diabetes, in addition to serving as a contraceptive, laxative, purgative, and for treating jaundice, filarial worm infection, hepatitis, etc.[17-21]

Jatropha multifida Linn., commonly called Coral Bush, is a plant belonging to the family Euphorbiaceae.[22, 23] It typically grows to a height of 3-5 m but can reach 8-10 m under favourable conditions.[24] Ethno-medicinally, the latex of this plant has been documented to be used for curing thrush on babies' tongues and also for treating infected wounds and skin infections. In addition, the seed and seed oil have purgative properties.[22] The insecticidal activities of *J. multifida* have also been reported.[25]

Mallotus oppositifolius (Euphorbiaceae) is an open shrub with elongated branches that may be curved, pendulous, or ascending.[26] Commonly referred to as "Kamala" in English, it also has numerous local names in Nigeria. It is an edible plant consumed in the south-eastern part of Nigeria, where its seed is used as a special soup thickener. Its insecticidal, antidysentery, antimalarial, and anti-inflammatory properties have been documented.[27-29]

Tabernaemontana pachysiphon Stapf. (Apocynaceae) is a plant that thrives in the understory of light forests across regions such as Ghana, both northern and southern Nigeria, western Cameroon, and the Republic of Congo (Brazzaville).[28] It is popularly called "Giant Pinwheel flower".[30] It has been documented to possess antimicrobial, anti-ulcer, and opiate receptor-binding activities .[28, 31, 32] Furthermore, the bark is known to be useful in treating anaemia and ulcers.[31]

Uvaria chamae, a member of the Annonaceae family, is a climbing medicinal plant. It grows naturally in the savannah and rainforest regions of West Africa and other tropical areas of the world.[33] Commonly referred to as 'finger root' or 'bush banana' in English, it also goes by different names in native languages.[33-35] *U. chamae* has several local uses.[34, 36-41] Its insecticidal activity on some selected stored-product insect pests has been reported.[36] There have been public campaigns against the indiscriminate use of synthetic chemicals on edible products, advocating instead for safer and healthier alternatives such as botanicals. Nevertheless, several toxicological and histopathological anomalies, such as necrosis, have been reported from the use of some plant materials at high concentrations.[2, 42, 43] Since these plants are consumed by humans either directly or indirectly, it is necessary to determine how medically safe they are.

Despite their well-established medical benefits and post-harvest effectiveness against pests, the toxicological and histopathological impacts of *U. chamae* root bark, *M. oppositifolius* leaf, *T. pachysiphon* leaf, *J. multifida* stem bark, and *A. djalonensis* stem bark have been poorly studied. Hence, the current research aimed to investigate the toxicity and histopathological implications of these plant materials in BALB/c mice.

2 Methods

Fresh samples of *Anthocleista djalonensis* stem bark, *Jatropha multifida* stem-bark, *Mallotus oppositofolius* leaf, *Tabernaemontana pachysiphon* leaf, and *Uvaria chamae* rootbark were collected in October from the Botanical Garden of Ekiti State University, Ado-Ekiti, Nigeria. All plant samples were taxonomically identified and authenticated by the Curator in the Department of Plant Science and Biotechnology, Faculty of Science, Ekiti State University, Nigeria. The voucher specimens numbered UHAE-20191033, 20191034, 20191035, 20191036 and 20191037 for *A. djalonensis* A. Chev (Gentianaceae), J. *multifida* Linn. (Euphorbiaceae), *M. oppositofolius* (Geiseler) Müll. Arg (Euphorbiaceae), *T. pachysiphon* Stapf. (Apocynaceae), and *U. chamae* P. Beauv (Annonaceae), respectively were deposited in the University's herbarium. The plant materials were air-dried at room temperature (27°C ± 2°C) to a constant weight on the bench in the laboratory for 30 days and pulverized into powder using a Binatone electric grinder (Model: BLG-402). Five hundred grams of each pulverized part were separately soaked in 2.5 L of 99-100% analytical grade ethanol for 72 hr and later decanted and re-soaked

until all the compounds of the plant were extracted. Ethanol was used due to its edible properties, economic viability, and being environmentally safer compared to other solvents.[44] Meanwhile, the extract was stirred every 24 hours to ensure proper dissolution of the active ingredients before decantation. After 72 hours, Whatman No. 1 filter paper was used to filter and the filtrate obtained was concentrated using a rotary evaporator (Heidolph, Germany) at 35℃. The concentrated extracts were further subjected to evaporation by lyophilization to remove traces of residual solvent. Yields of 20%, 17%, 21%, 23%, and 25% were obtained for *A. djalonensis*, *J. multifida, M. oppositofolius*, *T. pachysiphon*, and *U. chamae*, respectively. The extracts were stored at 4℃ in well-labelled air-tight containers for further use.[7] Stock solutions were prepared as described by guidelines.[45]

Experimental Animals and Housing Conditions

Following ethical approval by the Office of Research, Development and Innovation, Ekiti State University (ORD/EKSU/EAC/24/197), 33 healthy female (nulliparous and non-pregnant) experimental BALB/c mice weighing between 21.5 g and 28.0 g were obtained from the Animal House of the University's College of Medicine. The animals were housed in clean plastic cages under natural light and dark cycles at room temperature with free access to clean water and a standard rodent diet (Pfizer Feeds Plc., Nigeria). Before the experiment, the animals were allowed to acclimatize under these conditions for 5 days (Organization for Economic Cooperation and Development.[46] The experimental procedure was consistent with the ethical standards outlined by the National Research Council guidelines for the care and use of laboratory animals.[47]

Acute Oral Toxicity Test

The mice were randomly divided into 11 groups. Each group had three mice (n = 3). Group A (Control) was administered orally with vehicle (0.5 mL of distilled water) while the test groups were administered appropriate volumes of ethanol plant extracts at single doses of 300 and 2000 mg/kg according to Organization for Economic Cooperation and Development guidelines. [46] The experimental mice were denied food but not water for 3-4 hours before dosing. Following an overnight fast, the mice were weighed using an electronic precision weighing balance (Model SF-400A). The test substances were administered by gavage using an oral canula. Thereafter, the mice were deprived of food for 1-2 hours. [46] They were individually observed after treatment at intervals of 30 minutes for the first 24 hours. The mice were then observed for a period of 14 days for signs of evident toxicity. The body weights were measured on days 1, 7, and 14.[46] The experimental mice were dosed according to their respective body weight. On day 15, a mid-line incision was made via the anterior abdominal wall under ether anaesthesia. Two millilitres of whole blood samples were obtained from overnight fasted mice by cardiac puncture into well-labelled non-heparinized bottles. The animals were instantly euthanised, and the liver and kidney were collected and preserved in 10% neutral buffered formalin for gross pathological screenings.

Biochemical Analyses

The whole blood samples were allowed to sit undisturbed for 30 min at room temperature to allow for clotting. The clotted blood was centrifuged at 1000 × g for 10 min at 4℃. Following centrifugation, the supernatants were immediately transferred into sterile microcentrifuge tubes using a clean pipette and frozen at -15℃. The samples were analyzed for the expression of ALT, AST, ALP, total protein (TP), urea, and creatinine using commercial kits (Randox Test Kits, Germany).[2]

Histopathological Analysis

The fixed liver and kidney tissues were processed according to the general technique of tissue processing as described by Jensen et al.[48] Paraffin-embedded tissues were sectioned at 4-5 µm thickness using a rotary microtome (Model: Microm HM 325) and stained with haematoxylin and eosin (H & E).[49] Excess stain was removed with running tap water. The sections were cleared in xylene and allowed to dry. After clearing in xylene, Canada balsam was added, and coverslips were placed on the slides. The slides were placed in the oven at 40˚C. The slides were removed from the oven and allowed to cool. Each slide was observed under a digital microscope equipped with a camera (Model: OMAX 40X-2000X), and photomicrographs of the tissues were taken.

Statistical Analyses

Data on body weight of mice and biochemical analyses were subjected to one-way ANOVA using IBM SPSS 27.0.1 version. Results were presented as mean ± standard error, with statistical significance determined at $p < 0.05$.

3 Results

Acute Oral Toxicity Test

There was no sign of toxicity or death before the termination of the experiment. Organs of test animals were subjected to gross necropsy examination, and evidence of gross pathology was absent. The individual mean values of body weights of mice fed with different ethanol extracts at different dosages for 14 days are

presented in Table 1. Even though there was a gradual increase in the body weights of the mice, there were no significant differences ($p > 0.05$) in the test groups relative to the control.

Biochemical Analyses

Table 2 shows the toxicological effects of *A. djalonensis* stem bark, *J. multifida* stem bark, *M. oppositifolius* leaf, *T. pachysiphon* leaf, and *U. chamae* root bark on liver enzymes and TP of BALB/c mice. The liver activities of AST, ALT, ALP, and TP in mice fed with 0.5 mL of distilled water (control), 300 mg/kg, and 2000 mg/kg of the test extracts were not significantly different ($p > 0.05$) in serum levels. Similarly, Table 3 reveals the effects of the test extracts on kidney biochemical parameters (urea and creatinine) of BALB/c mice. There were no significant alterations ($p > 0.05$) in the parameters across all the study groups. The values obtained were within the normal range of mouse biochemistry.

Effects of 300 mg/kg of Different Plant Extracts on the Kidney of BALB/c Mice

Figure 1 Plates 1 A-F show the results of the mice administered 0.5 mL of vehicle and 300 mg/kg of A. djalonensis stem bark, J. multifida stem bark, M. oppositifolius leaf, T. pachysiphon leaf, and U. chamae root bark. A regular histoarchitecture of the renal tissue was observed across all study groups, featuring the glomeruli with intact Bowman's capsules and essentially normal renal tubules.

Effects of 2000 mg/kg of Different Plant Extracts on BALB/c Mice Kidney

The histology results of mice given 0.5 mL of distilled water and 2000 mg/kg of A. djalonensis stem bark, J. multifida stem bark, M. oppositifolius leaf, T. pachysiphon leaf, and U. chamae root bark are shown in Figure 2, Plates 2 A-F. The structure of the kidney showed essentially normal histoarchitecture of the renal tissues relative to the control group.

Effects of 300 mg/kg of Different Plant Extracts on the Liver of BALB/c Mice

As seen in Figure 3, Plates 3 A-F, histological examination of liver sections of mice administered 0.5 mL of vehicle and 300 mg/kg of *A. djalonensis* stem bark, *J. multifida* stem bark, *M. oppositifolius* leaf, *T. pachysiphon* leaf, and *U. chamae* root bark showed hepatic tissues arranged into normal lobules with the hepatocytes radiating from the central veins. Within each lobule, normal hepatocytes were arranged into hepatic cords separated by adjacent sinusoids.

Table 1 Change in body weight of mice treated with test plants for 14 days

Groups	Dosages (mg/kg)	Day 1	Day 7	Day 14
A	Control (0.5 ml)	22.67 ± 1.04^a	23.17 ± 1.10^a	23.90 ± 1.04^a
B1	300	25.30 ± 0.72^a	25.43 ± 0.86^a	26.40 ± 0.87^a
B2	2000	25.37 ± 0.90^a	25.60 ± 0.82^a	26.10 ± 0.76^a
C1	300	25.77 ± 0.32^a	26.17 ± 0.52^a	26.60 ± 0.40^a
C2	2000	26.53 ± 1.37^a	26.87 ± 1.32^a	27.33 ± 1.04^a
D1	300	24.77 ± 0.67^a	25.13 ± 0.67^a	25.83 ± 0.67^a
D2	2000	25.87 ± 0.15^a	26.13 ± 0.21^a	26.90 ± 0.20^a
E1	300	23.22 ± 1.20^a	24.07 ± 1.27^a	24.83 ± 1.29^a
E2	2000	24.80 ± 0.82^a	25.40 ± 0.76^a	26.13 ± 0.71^a
F1	300	25.93 ± 0.84^a	26.47 ± 0.98^a	27.57 ± 0.99^a
F2	2000	26.23 ± 0.31^a	26.63 ± 0.31^a	27.17 ± 0.15^a

*Each value is the mean ± standard error of three replicates. Means with different superscripts in each column are significantly different ($p < 0.05$) using the Tukey test.
A- Control
B- *A. djalonensis* stem-bark extract
C- *J. multifida* stem-bark extract
D- *M. oppositifolius* leaf
E- *T. pachysiphon* leaf
F- *U. chamae* root bark

Effects of 2000 mg/kg of Different Plant Extracts on the Liver of BALB/c Mice

The histology of the hepatic tissues of mice in both the treated (2000 mg/kg) and control groups (Figure 4 Plates 4 A-F) showed well-preserved histoarchitectures, with hepatocytes radiating from the central veins and arranged in a regular sinusoidal pattern.

Table 2 Serum biochemical parameters of the liver of BALB/c mice fed plant extracts

Groups	AST (u/L) (54-298)	ALT (u/L) (17-77)	ALP (u/L) (35-96)	Total Protein (g/dL) (3.5-7.2)
A (Control)	58.31 ± 0.11[a]	27.91 ± 0.96[a]	41.80 ± 0.88[a]	3.58 ± 0.01[a]
B1 (*A. djalonensis* 300 mg/kg)	70.61 ± 0.32[a]	28.18 ± 0.31[a]	52.43 ± 3.26[a]	3.68 ± 0.02[a]
B2 (*A. djalonensis* 2000 mg/kg)	81.17 ± 0.21[a]	29.26 ± 0.72[a]	46.99 ± 0.44[a]	3.71 ± 0.09[a]
C1 (*J. multifida* 300 mg/kg)	69.81 ± 0.19[a]	27.32 ± 1.53[a]	54.74 ± 1.69[a]	3.59 ± 0.03[a]
C2 (*J. multifida* 2000 mg/kg)	72.51 ± 0.28[a]	27.88 ± 0.90[a]	42.33 ± 1.71[a]	4.89 ± 0.01[a]
D1 (*M. oppositifolius* 300 mg/kg)	71.91 ± 0.08[a]	30.66 ± 2.71[a]	71.32 ± 0.6[a]	5.81 ± 0.02[a]
D2 (*M. oppositifolius* 2000 mg/kg)	82.76 ± 0.51[a]	31.92 ± 1.06[a]	41.44 ± 1.96[a]	5.94 ± 0.08[a]
E1 (*T. pachysiphon* 300 mg/kg)	60.01 ± 0.05[a]	28.81 ± 0.94[a]	63.61 ± 3.94[a]	4.46 ± 0.01[a]
E2 (*T. pachysiphon* 2000 mg/kg)	80.96 ± 0.23[a]	29.17 ± 1.06[a]	55.40 ± 2.61[a]	4.38 ± 0.00[a]
F1 (*U. chamae* 300 mg/kg)	89.46 ± 0.04[a]	32.66 ± 1.76[a]	68.33 ± 0.48[a]	5.94 ± 0.04[a]
F2 (*U. chamae* 2000 mg/kg)	82.61 ± 0.82[a]	32.81 ± 1.38[a]	60.26 ± 1.02[a]	6.02 ± 0.02[a]

*Each value is the mean ± standard error of three replicates. Means with different superscripts in each column are significantly different ($p < 0.05$) using Tukey's test.

Table 3 Serum biochemical parameters of the kidney of mice fed plant extracts

Groups	Urea (mg/dL) (8-33)	Creatinine (mg/dL) (0.2-0.9)
A (Control)	18.02 ± 0.50[a]	0.22 ± 0.00[a]
B1 (*A. djalonensis* 300 mg/kg)	21.81 ± 2.84[a]	0.30 ± 0.05[a]
B2 (*A. djalonensis* 2000 mg/kg)	22.02 ± 2.02[a]	0.35 ± 0.06[a]
C1 (*J. multifida* 300 mg/kg)	19.61 ± 1.14[a]	0.41±0.04[a]
C2 (*J. multifida* 2000 mg/kg)	21.40 ± 2.96[a]	0.49 ± 0.03[a]
D1 (*M. oppositifolius* 300 mg/kg)	20.69±1.02[a]	0.30 ± 0.05[a]
D2 (*M. oppositifolius* 2000 mg/kg)	23.58 ± 1.96[a]	0.43 ± 0.11[a]
E1 (*T. pachysiphon* 300 mg/kg)	20.86 ± 0.61[a]	0.44 ± 0.02[a]
E2 (*T. pachysiphon* 2000 mg/kg)	21.26 ± 8.07[a]	0.45 ± 0.07[a]
F1 (*U. chamae* 300 mg/kg)	22.74 ± 2.20[a]	0.33 ± 0.09[a]
F2 (*U. chamae* 2000 mg/kg)	23.36 ± 1.96[a]	0.41 ± 0.01[a]

*Each value is the mean ± standard error of three replicates. Means with different superscripts in each column are significantly different ($p < 0.05$) using Tukey's test.

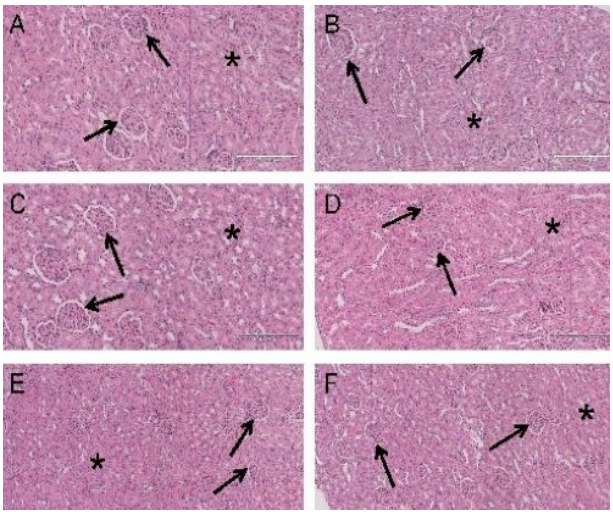

Figure 1 Plate 1: Photomicrographs of sections of the kidney of mice

Control administered with 0.5 ml of vehicle (Distilled water)
300 mg/kg *Anthocleista djalonensis* stem-bark extract
300 mg/kg *Jatropha multifida* stem-bark extract
300 mg/kg *Mallotus oppositifolius* leaf extract
300 mg/kg *Tabernaemontana pachysiphon* leaf extract
300 mg/kg *Uvaria chamae* root-bark extract
Arrows (→) show glomeruli while asterisks (*) show renal tubules
Magnification = 100x; Scale bar = 20 µm

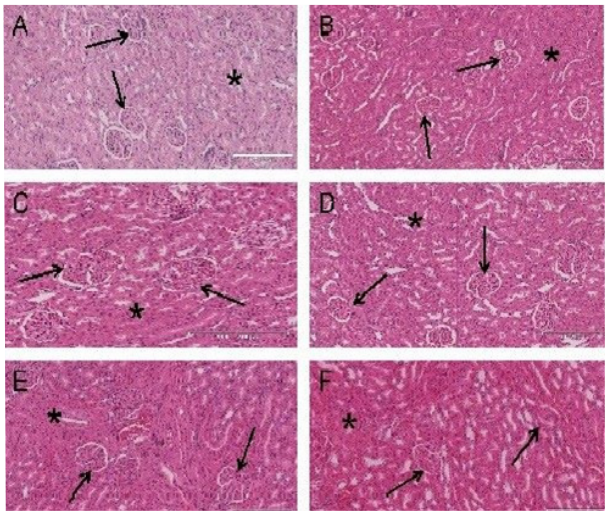

Figure 2 Plate 2: Photomicrographs of sections of the kidney of mice

A-Control administered with 0.5 ml of vehicle (Distilled water)
B- 2000 mg/kg *Anthocleista djalonensis* stem-bark extract
C- 2000 mg/kg *Jatropha multifida* stem-bark extract
D-2000 mg/kg *Mallotus oppositifolius* leaf extract
E- 2000 mg/kg T*abernaemontana pachysiphon* leaf extract
F- 2000 mg/kg *Uvaria chamae* root-bark extract
Arrows (→) show glomeruli while asterisks (*) show renal tubules
Magnification = 100x; Scale bar = 20 µm

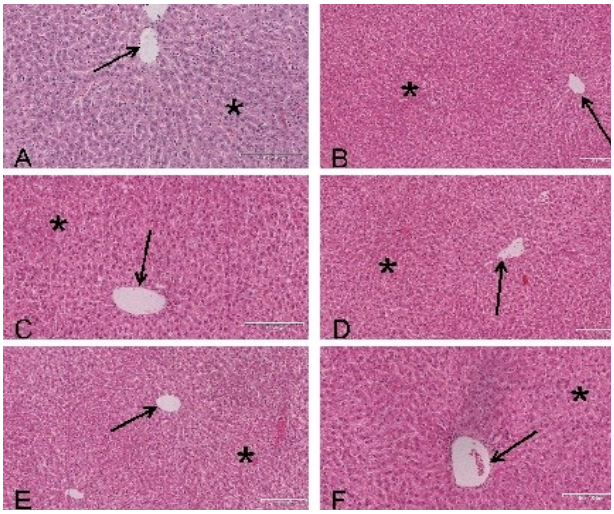

Figure 3 Plate 3: Photomicrographs of sections of the liver of mice

Control administered with 0.5 ml of vehicle (Distilled water)
300 mg/kg *Anthocleista djalonensis* stem-bark extract
300 mg/kg *Jatropha multifida* stem-bark extract
300 mg/kg *Mallotus oppositifolius* leaf extract
300 mg/kg *Tabaernaemontana pachysiphon* leaf extract
300 mg/kg *Uvaria chamae* root-bark extract
Arrows (→) show the central vein while asterisks (*) show the hepatocytes.
Magnification = 100x; Scale bar = 20 µm

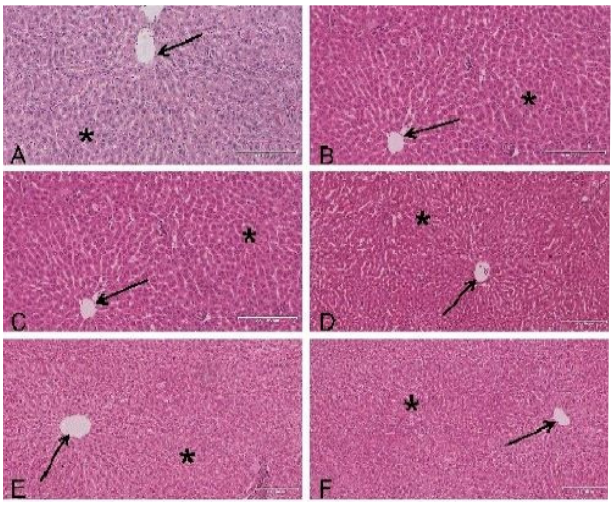

Figure 4 Plate 4: Photomicrographs of sections of the liver of mice

A- Control administered with 0.5 ml of vehicle (Distilled water)
B- 2000 mg/kg *Anthocleista djalonensis* stem-bark extract
C- 2000 mg/kg *Jatropha multifida* stem-bark extract
D- 2000 mg/kg *Mallotus oppositifolius* leaf extract
E- 2000 mg/kg *Tabaernaemontana pachysiphon* leaf extract
F- 2000 mg/kg *Uvaria chamae* root-bark extract
Arrows (→) show the central vein while asterisks (*) show the hepatocytes.
Magnification = 100x; Scale bar = 20 µm

4 Discussion

Assessment of biochemical parameters in the blood can be used to determine the extent of the harmful effects of a foreign compound, including plant-derived compounds, in humans or animals.[42] AST, ALT, and ALP are important marker enzymes in organs such as the liver and kidney, which are usually released into the serum when there is damage to the hepatic and nephritic membranes due to chemical attack.[50] Furthermore, they are pointers used to diagnose and examine the progression of a disease as well as to monitor or detect hepatotoxicity and nephrotoxicity that may arise from the use of drugs or substances.[51, 52] ALP, a marker enzyme found in the plasma membrane and endoplasmic reticulum,[53] is frequently used to assess the integrity of the plasma membrane.[54] The detected normal concentrations of ALP activities in the liver of treated mice and the control group suggest that there was no obstruction to the movement of the required ions or molecules across the plasma membrane. Likewise, the non-significant effects of ALT and AST in the test groups following the administration of the extracts, when compared to the control, are an indication that the livers of the animals were not damaged. TP is also a useful guide for the impairment of the functional capacity of the liver and kidneys.[42] The normal level of TP observed in the treated groups indicates the absence of non-liver disorders and nephritic damage. Similar observations were reported by Akomolafe et al.[55] in the toxicological effects of aqueous extracts of African walnut (*Tetracarpidium conophorum*) leaf in rats.

Blood urea and creatinine are key indicators of renal function. Urea, the main nitrogen byproduct of protein metabolism,[42] is predominantly excreted through the kidneys.[43] Creatinine is a breakdown product of creatine phosphate, which is routinely produced by muscles and protein metabolism, and is eliminated from the body by the kidneys. Creatinine is the most commonly used indicator of kidney function. Thus, any kidney impairment will make the kidneys inefficient in eliminating both urea and creatinine, which will lead to their buildup in the bloodstream. It was observed that none of the test extracts changed the biochemical parameters of the kidneys, as there was no significant increase or accumulation of urea and creatinine in the serum which indicated healthy kidneys. Consequently, the results of the present investigation showed that the administration of the test extracts at 300 mg/kg and 2000 mg/kg was not toxic to the liver or kidneys of the mice, based on ALT, AST, ALP, TP, urea, and creatinine levels, as they appeared in normal concentrations in the serum. Independent studies by Nwosu et al.[50] and Emordi et al.[52] in albino rats treated with methanolic extract of *Dennettia tripetala* seed and hydroethanolic root extract of *Uvaria chamae* further confirmed the findings of the present investigation. In addition, it was observed that there were no changes in physical activities and no signs of toxicity or death in both test groups and their controls before the termination of the experiment. It is also worth stating that there was no decline in body weights in all the represented groups.

The histopathological findings of the test extracts revealed that the livers of both the controls and test groups had well-preserved hepatocytes arranged in a regular sinusoidal pattern which is an indication that the test extracts did not have any damaging effect on the organs of the tested animals. The normal kidney architecture observed in the test animal groups also strongly implies normal kidney functions (ultrafiltration and selective absorption) which suggested that toxicity did not occur at any concentrations examined. Therefore, they are safe ($\leq$ 2000 mg/kg of treatment) for consumption. These observations are in agreement with previous studies by Akparie[56] and Nwosu et al.[50]

5 Conclusion

The findings of the present research provide scientific justification for the utilization of these plant extracts as stored product protectants. They were found to be non-toxic to BALB/c mice at all concentrations tested and, therefore, considered relatively safe. Future studies will focus on the isolation of active compounds in each plant. These may provide promising prospects for the use and commercialization of these plants as food storage biomaterials. Thus, there will be improved sustainability quality and shelf life of postharvest food, ultimately ensuring global food security.

Declarations

Acknowledgments
We would like to acknowledge the assistance of Mr. Omotayo in sourcing and authenticating the plants used in this study.

Artificial Intelligence Disclosure
The authors confirm that no artificial intelligence (AI) tools were used in the preparation of this manuscript.

Authors' Contributions
Tejumade Mary Philip-Attah was responsible for data collection and writing the paper.
Olumuyiwa Temitope Omotoso supervised the project and handled proof-reading.
Margaret Olutayo Alese conducted data analysis and assisted with proof-reading.
Olusola Michael Obembe contributed to proof-reading.

Availability of Data and Materials
The data that support the findings of this study are available upon request from the corresponding author.

Conflict of Interest
The authors declare no conflict of interest.

Consent for Publication
All authors have read and approved the final manuscript and have provided their consent for publication.

Ethical Considerations
The proposal for this study was approved by the Office of Research, Development, and Innovation, Ekiti State University, Nigeria under the Code of Ethics ORD/EKSU/EAC/24/197. The researchers adhered to all the principles recommended by the National Research Council.

Funding
None.

References

1. Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. African journal of traditional, complementary and alternative medicines. 2013;10(5):210-29.
2. Atsafack SS, Kuiate J-R, Mouokeu RS, Koanga Mogtomo ML, Tchinda AT, De Dieu TJ, et al. Toxicological studies of stem bark extract from Schefflera barteri Harms (Araliaceae). BMC complementary and alternative medicine. 2015;15(1):44.
3. Bashir EM, El Shafie HA. Insecticidal and antifeedant efficacy of Jatropha oil extract against the desert locust, Schistocerca gregaria (Forskal)(Orthoptera: Acrididae). Agriculture and Biology Journal of North America. 2013;4(3):260-7.
4. Adesina J, Jose A, Adetuyi O, Olorunfemi D. Larvicidal activity of Phyllanthus fraternus powder in suppressing Dermestes maculatus Degeer (Coleoptera: Dermestidae) infestation on smoked African catfish (Clarias gariepinus). International Journal Aquaculture. 2014;4:67-72.
5. Adesina JM, Jose AR, Rajashekar Y. Bio-efficacy of Clerodendrum capitatum (Willd) Schumachet. Thonn.(Lamiales: Verbenaceae) against Dermestes maculatus De Geer, 1774 (Coleoptera: Dermestidae) larvae infestation on smoked catfish Claria gariepinus (Burchell, 1822)(Siluriformes: Clariidae). Brazilian Journal of Biological Sciences. 2016;3(5):e214-e.
6. Negbenebor H, Makanjuola W, Denloye A, Nura S. Toxicity of powdered and ethanolic extracts of Uvaria chamae (Annonaceae) Bark on selected stored product insect pests. African Journal of Biotechnology. 2018;17(11):350-5.
7. Philip-Attah TM. Evaluation of ethanolic extracts of Piper guineense, Dennettia tripetala, and Capsicum frutescens as protectant of smoked fish, Clarias gariepinus (Pisces: Clariidea) against Dermestes maculatus (Coleoptera: Dermestidae). The Journal of Basic and Applied Zoology. 2019;80(1):7.
8. Ileke KD. Responses of two plant-derived bioinsecticides as protectants of smoke-dried catfish, Clarias gariepinus [Pisces: Clariidae] against hide beetle, Dermestes maculatus (De Geer) [Coleoptera: Dermestidae]. Bulletin of the National Research Centre. 2021;45(1):28.
9. De Wilde J. Novitates Gabonenses 73. A new species of Anthocleista (Gentianaceae) from Gabon. Blumea-Biodiversity, Evolution and Biogeography of Plants. 2011;56(1):1-3.
10. Leeuwenberg A. Anthocleista grandiflora. Flowering plants of Africa 52-2 (1993) pl 2080, 3 pp1993.
11. Hyde MA, Wursten BT, Ballings P, Coates-Palgrave M. Anthocleista. In: Flora of Zimbabwe: Genus page [Internet]. 2015
12. Keay RWJ. Trees of nigeria: Oxford University Press; 1990.
13. Anyanwu G. Impact of Anthocleista vogelii root bark ethanolic extract on weight reduction in high carbohydrate diet induced obesity in male wistar rats. 2013.
14. Popoola O. Phytochemical status of different solvent extracts of Anthocleista djalonensis A. Chev leaves. International Annals of Science. 2020;8(1):62-9.
15. Dalziel JM. The useful plants of west tropical Africa. 1937.
16. Ateufack G, Nguelefack TB, Wabo HK, Tane P, Kamanyi A. Antiulcerogenic activity of 1-hydroxy-3, 7, 8-trimethoxyxanthone isolated from the methanol extract of Anthocleista vogelii PLANCH. in rats. Ulcers. 2014;2014(1):172096.
17. Okoli A, Iroegbu C. Evaluation of extracts of Anthocleista djalonensis, Nauclea latifolia and Uvaria afzalii for activity against bacterial isolates from cases of non-gonococcal urethritis. Journal of ethnopharmacology. 2004;92(1):135-44.
18. Aiyeloja A, Bello O. Ethnobotanical potentials of common herbs in Nigeria: A case study of Enugu state. Educational Research and Reviews. 2006;1(1):16.
19. Kadiri AB. An examination of the usage of herbal contraceptives and abortifacients in Lagos State, Nigeria. Ethnobotanical leaflets. 2009;2009(1):16.
20. Musa A, Yusuf G, Ojogbane E, Nwodo O. Screening of eight plants used in folkloric medicine for the treatment of typhoid fever. Journal of Chemical and Pharmaceutical Research. 2010;2(4):7-15.
21. Olubomehin O, Abo K, Ajaiyeoba E. Alpha-amylase inhibitory activity of two Anthocleista species and in vivo rat model anti-diabetic activities of Anthocleista djalonensis extracts and fractions. Journal of Ethnopharmacology. 2013;146(3):811-4.
22. Aiyelaagbe OO, Gloer JB. Japodic acid, a novel aliphatic acid from Jatropha podagrica Hook. Records of Natural Products. 2008;2(4).
23. Anani K, Adjrah Y, Ameyapoh Y, Karou SD, Agbonon A, De Souza C, et al. Antimicrobial, anti-inflammatory and antioxidant activities of Jatropha multifida L.(Euphorbiaceae). Pharmacognosy Res. 2016;8(2):142-6.
24. Van Welzen PC, Sweet FS, Fernández-Casas FJ. A revision of Jatropha (Euphorbiaceae) in Malesia. Blumea-Biodiversity, Evolution and Biogeography of Plants. 2017 1;62(1):58-74. Adebowale K, Adedire C. Chemical composition and insecticidal properties of the underutilized Jatropha curcas seed oil. African

Journal of Biotechnology. 2006;5(10):901.

25. Adekunle A, Ikumapayi A. Antifungal property and phytochemical screening of the crude extracts of Funtumia elastica and Mallotus oppositifolius. West Indian Medical Journal. 2006;55(4):219.
26. Oke O, Oyebode G, Onifade E. Evaluation of contact activities of Leaf extracts from four plant species Against Sitophilus zeamais motschulsky (Coleoptera: Curculiondae). Serangga; 2014.
27. Kabran F, Maciuk A, Okpekon T, Leblanc K, Seon-Meniel B, Bories C, et al. Phytochemical and biological analysis of Mallotus oppositifolius (Euphorbiaceae). Planta Medica. 2012;78(11):PI381.
28. Iwu MM. African medicinal plants. CRC Press, Maryland Jamkhande, PG, Ajgunde, BR, & Jadge, DR (2017) Annona cherimola Mill(Custard apple): A review on its plant profile, nutritional values, traditional claims and ethnomedicinal properties Oriental Pharmacy and Experimental Medicine. 1993;17(3):189-201.
29. Duru C, Mbata T. The antimicrobial activities and phytochemical screening of ethanolic leaf extracts of Hedranthera barteri Hook and Tabernaemontana pachysiphon Stapf. J Dev Biol Tissue Eng. 2010;2(1):1-4.
30. Uwumarongie OH, Onwukaeme ND, Igbe I. Phytochemical Analysis and Hypoglycaemic Activity of the Methanol Stem Bark Extract of Tabernaemontana pachysiphon Stapf (Apocynaceae): https://doi. org/10.26538/tjnpr/v1i4. 4. Tropical Journal of Natural Product Research (TJNPR). 2017;1(5):213-6.
31. Uwumarongie O, Onwukaeme D, Obasuyi O. Antimicrobial activity of the methanolic leaf extract of Tabernaemontana pachysiphon stapf.(Apocynaceae). Nigerian Journal of Natural Products and Medicine. 2007;11:23-5.
32. Uwumarongie H, Onwukaeme D, Bafor E. Antiulcer effects and elements of Tabernaemontana pachysiphon stem bark. Niger J Pharm Res. 2008;7:69-75.
33. Emeka EJ, Oluwatoyin AE, Adekunle OI, Ignis IO. Preliminary phytochemical screening and evaluation of hypoglycemic properties of the root extract of Uveria chamae. Bangladesh Journal of Pharmacology. 2015;10(2):326-31.
34. James O, Godwin EU, Otini IG. Uvaria chamae (Annonaceae) plant extract neutralizes some biological effects of Naja nigricollis snake venom in rats. Bri J Pharmacol Toxicol. 2013;4:41-50.
35. Olumese F, Onoagbe I, Eze G, Omoruyi F. Safety assessment of Uvaria chamae root extract: acute and subchronic toxicity studies. Journal of African Association of Physiological Sciences. 2016;4(1):53-60.
36. Iwu E. Ethnobotanical importance of some Nigerian plants. Jour Ethnomedicine. 1993;55:893-906.
37. Okwu D. Phytochemical analysis and antimicrobial activity screening of aqueous and ethanolic root extracts of Uvaria chamae Beuv and Cnestis ferruginea D. C. J Chem Soc Nigeria. 2004;29:112-4.
38. Igoli J, Ogaji O, Tor-Ayiin T, Igoli N. Traditional medicine practice amongst the Igede people of Nigeria. Part II. African Journal of Traditional, Complementary and Alternative Medicines. 2005;2(2):134–52-–52.
39. Okokon J, Ita B, Udokpoh A. The in-vivo antimalarial activities of Uvaria chamae and Hippocratea africana. Annals of Tropical Medicine & Parasitology. 2006;100(7):585-90.
40. Okwu DE. Nigerian medicinal plants I. Medicinal and Aromatic Plant Science and Biotechnology. 2007;1(1):90-6.
41. Oluremi B, Osungunna M, Omafuma O. Comparative assessment of antibacterial activity of Uvaria chamae parts. African Journal of Microbiology Research. 2010;4(13):1391-4.
42. Odeyemi O, Masika P, Afolayan A. A review of the use of phytochemicals for insect pest control. African Plant Protection. 2008;14(1):1-7.
43. Ileke KD, Odeyemi OO, Ashamo MO, Oboh G. Toxicological and histopathological effects of cheese wood, alstonia boonei de wild stem bark powder used as cowpea protectant against cowpea bruchid, callosobruchus maculatu (fab.)[coleoptera: Chrysomelidae] on albino rats. Ife Journal of Science. 2014;16(1):23-33.
44. Erhirhie E, Ekene NE, Ajaghaku D. Guidelines on dosage calculation and stock solution preparation in experimental animals' studies. 2014.
45. No OT. 436: Acute inhalation toxicity–acute toxic class method. OECD Guidelines for the Testing of Chemicals, Section. 2009 ;4.
46. Care IoLARCo, Animals UoL. Guide for the care and use of laboratory animals: US Department of Health and Human Services, Public Health Service, National …; 1986.
47. Jensen K. Theory and practice of histological techniques. American Association of Neuropathologists, Inc.; 2008.
48. Silva A, Bambirra E, Oliveira A, Souza P, Gomes D, Vieira E, et al. Protective effect of bifidus milk on the experimental infection with Salmonella enteritidis subsp. typhimurium in conventional and gnotobiotic mice. Journal of Applied Microbiology. 1999;86(2):331-6.
49. Chinaru Nwosu L, Olukayode Adedire C, Oludele Ogunwolu E, Olufemi Ashamo M. Toxicological and histopathological effects of Dennettia tripetala seed used as grain protectant, food, and medicine. Food Quality and Safety. 2017;1(3):211-20.
50. Oluba O, Adeyemi O, Ojieh G, Adebisi K, Isiosio I, Aboluwoye C. Effects of dietary cholesterol on some serum enzymes. 2008.
51. Oluba OM, Adeyemi O, Ojieh GC, Adebisi KE, Isiosio IO, Aboluwoye CO. Effects of dietary cholesterol on some serum enzymes. Journal of Medical Sciences (Pakistan). 2008;8(4):390-94.
52. Shahjahan M, Sabitha K, Jainu M, Devi CS. Effect of Solanum trilobatum against carbon tetra chloride induced hepatic damage in albino rats. Indian Journal of Medical Research. 2004;120:194-8.
53. Akanji MA, Olagoke OA, Oloyede OB. Effect of chronic consumption of metabisulphite on the integrity of the rat kidney cellular system. Toxicology. 1993;81(3):173-9.
54. Akomolafe SF, Oboh G, Oyeleye SI, Olasehinde TA. Toxicological effects of aqueous extract from African walnut (Tetracarpidium conophorum) leaves in rats. Journal of Evidence-Based Complementary & Alternative Medicine. 2017;22(4):919-25.
55. Akparie S. General Veterinary Pathology, Stirling–Horden publishers (Nig) Ltd. Pp136. 2004.