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Research Article

Toxicological Evaluation of the Ethanolic Extract the Tropical Medicinal Plant Ximenia americana in Albino Wistar Rats

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Abstract:

The present work comprises a preliminary phytochemical analysis and toxicological evaluation of the ethanolic extract of the dry leaves of the tropical medicinal plant Ximenia americana in albino Wistar rats. The results of the phytochemical analysis revealed the presence of tannins, flavonoids, saponins, sterols, triterpenes and alkaloids. The repeated oral administration of the ethanolic extract at dose rates of 100, 200 and 400 mg / kg body weight did not produce detectable clinical changes or significant gross or histopathological alterations in experimental rats when the extract was daily given for three weeks. There were no significant changes in hematological parameters including Hb concentration, PCV, RBCs count, MCH, MCHC and PLT count when the ethanolic extract was given at 100 and 200mg /kg body weight. However, a significant increase in RBCs count and other red blood indices was observed when the extract was given at 400 mg/kg body weight. In addition, the plasma biochemical parameters including total plasma protein, albumin, urea nitrogen, creatinine and the plasma enzyme activity of aspartate aminotransferase (AST) and alanine aminotransferase were not significantly affected in experimental rats receiving the ethanolic extract at 100, 200 and 400 mg /kg body weight. The mean body weight was significantly increased in experimental rats receiving 100 mg/kg body weight of the ethanolic extract for three weeks. However, a decrease in mean body weight was observed when the extract was given at 400 mg/kg. It is concluded that the tropical medicinal plant X.americana has an almost negligible adverse effect on rats and therefore could safely be used in folk medicine for treatment of various type of infectious and neoplastic diseases.

Keywords: traditional (folk) medicine; medicinal plants; ximenia americana; sudan

Introduction

The therapeutic potential of numerous types of herbal plants has long been recognized in various countries throughout the ancient and recent history [1]. The type of plant species especially used for treatment of diseases in man and animals are customary designated as medicinal plants. Medicinal plants are widely used in folk or traditional (alternative) medicine for treatment of different types of infectious and neoplastic diseases in human patients particularly in rural areas mainly in developing countries in Africa, Asia and Latin America [2,3]. Nevertheless, the traditional use of medicinal plants has further expanded to include a number of developed countries such as the United Kingdom and many other countries in Europe, North America and Australia [4, 5]. It has been estimated that more than 80% of the total world's population still depends on herbal medicine for treatment of several types of diseases in different parts of the world [1].

The tropical plant *Ximenia americana* belongs to the family *Olacaceae*. It is a short shrub or small tree originally native in Southern America with a wide spread in Africa and many other continents. It is one of the most widely used medicinal plant as a traditional herbal remedy for various types of ailments in numerous countries all over the world. It is extensively used in Nigeria among the Hausa/Fulani communities for treatment of several diseases including malaria, leprotic ulcers and skin infections [6]. It is also used in folk medicine in many other West African countries such as Senegal, Guinea and Burkina Faso to treat various disorders such as oral diseases, inflammation, pain and fever [7-9]. The plant was also used for treatment of sleeping sickness in humans [10, 11] diarrhea and wounds [12] and intoxications [13]. The preparations of the branched leaf, bark, and root were used for treatment of headache, toothache, mumps and conjunctivitis [8,14]. The extract of the plant was also found to have an antimicrobial effect against many microbial organisms including *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida albicans*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and so many other bacterial and fungal organisms [6, 9, 12, 15-17].

The traditional use of *X. americana* as a herbal remedy in Sudan is commonly practiced by rural inhabitants in South Kordofan State and some other areas of Western parts of the country [18,19, 20, 21]. However, very little is currently known about the adverse effect of the

plant on human patients and experimental animals. The present investigation was therefore designed to perform a preliminary phytochemical screening and toxicological evaluation of the plant in albino Wistar rats given repeated daily oral doses of the ethanolic extract of the dry leaves for a three-week period of observation (sub-chronic toxicity).

Materials and Methods

Collection of plant material

Ximenia americana leaves were collected from natural forests in North Kordofan State, Sudan. The leaves were identified and authenticated by the scientific staff of the Medicinal and Aromatic Plants Research Institute - National Center of Research, Khartoum, Sudan. The leaves were cleaned and shade dried at room temperature **Preparation of Ethanolic Extract**. The dry leaves of *X.americana* were thoroughly grounded using a pestle and mortar. About 220 gm of the powdered leaves were extracted by soaking in 70 % ethanol for seventy two hours with daily filtration and evaporation [22]. Solvent was evaporated under reduced pressure to dryness using rotary evaporator apparatus. The yield of the extract was calculated as follows:

Weight of extract / Weight of sample X 100

The residue obtained was kept in dry clean bottle until used.

Phytochemical Screening

Preliminary phytochemical screening for the active constituents of the plant was carried out on the ethanolic extract using the methods described by Tease and Evans [23].

Experimental Animals

Twenty-four albino Wistar rats weighting between 82-135gm were obtained from the Experimental Animal Unit at the Faculty of Veterinary Medicine, University of Khartoum. They were housed in well-ventilated room with free access to water and food. They were given a seven-day period of adaptation to laboratory environment.

Experimental Design

The experimental rats were divided to four equal groups (n=6). Group 1 rats were kept as undosed controls. The ethanolic extract of X. americana was dissolved in distilled water and administered to the experimental groups as daily repeated oral doses of 100 mg/kg body weight /day (Group2), 200 mg/kg body weight/ day (Group 3) and 400 mg/kg body weight/ day (Group 4). The daily dosing of the extract continued via a stomach tube for a period of three weeks (sub-chronic). (Group2), 200 mg/kg body weight/ day (Group 3) and 400 mg/kg body weight/ day (Group 4). The daily dosing of the extract continued via a stomach tube for a period of three weeks (sub-chronic)

Clinical Observations and Laboratory Analysis

The rats were thoroughly observed for abnormal clinical changes throughout the experimental period (21 days). The body weight of rats was measured before dosing and at weekly intervals. Heparinized blood samples were collected by puncturing retro-orbital plexus using a capillary tube at day zero and day 21. The blood samples were immediately analyzed for hematological parameters including hemoglobin concentration (Hb), packed cell volume (PCV), red blood cell count (RBCs), white blood cell count (WBCs), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) by the use of Sysmex Automated Hematology Analyzer (KX-21N, Spain). Plasma was separated by centrifugation of blood at 2500 rpm for 15 minutes and stored at -20°C until analyzed for biochemical parameters including plasma total protein [24], albumin [25], urea (26) and creatinine [27] by using commercial kits (Randox Laboratories Limited UK). The plasma enzyme activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) was also measured by commercial kits (BioSystem SA Spain) according to the method of Reitman and Frankel [28]. Control and experimental rats were sacrificed on day 21 for detailed post –mortem examination. The whole carcasses and visceral organs were thoroughly examined for detectable gross lesions. Representative specimens of the liver, kidney, heart, intestine and spleen were fixed in 10% formal saline for routine histopathological processing and staining with haematoxylin and eosin (H&E) as described by Bancroft and Gamble [29].

Statistical Analysis

The results were analyzed using SPSS (Microsoft ver. 20, USA). Data was analyzed using multivariate analysis. The Significance of differences among the group were assessed using T-test. The data were expressed as mean ± standard deviation (STD). Level of significance was taken at ($P < 0.05$).

Results

Plant Extraction

The results of ethanolic extraction of the dry leaves of *X. americana* is shown in Table 1. A total of 220 gm of the leaves produced 62.546 gm of ethanolic extract. The yield percentage was 28.43 %.

Sample	Weight of sample	Weight of extract	Yield %
X. americana Leaves	220 gm	62.546 gm	28.43 %

Table 1: Final yield of ethanolic extract of X. americana dry leave

Phytochemical Analysis

Preliminary photochemical analysis of the ethanolic extract of the dry leaves of X. americana is shown in Table 2. The results revealed the presence of high, amounts of tannins and flavonoids, moderate amounts of saponins, sterols and triterpenes and lesser amounts of alkaloids. Other ingredients reported in literature such as cumarins, anthraquinone glycosides and cyanogenic glycosides were not detected in the ethanolic extract of X. americana leaves in the present stud

Constituent	*Result	Observations
Saponins	++	Foam
Alkaloids	+	Turbidity
Tannins	+++	Green black color + turbidity
Flavonoids	+++	Yellow color + creamy precipitates
Sterols	++	Green color
Triterpenes	++	Purple color
Cumarins	-	Not detectable

Anthraquinone glycosides	-	Not detectable
Cyanogenic glycosides	-	Not detectable

**** trace* (+) *moderate* (++) *high* (+++)**

Table 2. Basic phytochemical constituents of ethanolic extract of *X. americana leaves* (preliminary analysis)

Clinical Findings

No significant abnormal clinical changes were observed in control rats (Group 1) and in other experimental rats receiving repeated daily oral doses of the ethanolic extract of the dry leaves of *X. americana* at dose rates of 100 mg /kg body weight/day (Group 2), 200 mg /kg body weight /day (Group 3) and 400 mg/kg body weight/ day (Group 4) throughout the observation period (21 days).

Hematological Findings

The effect of administration of the ethanolic extract of *X. americana* leaves on some hematological parameters of experimental rats is shown in Table 3.

	Group 1 (Control)	**Group 2** (100 mg/kg/day)	**Group3** (200 mg/kg/day)	**Group 4** (400 mg/kg/day)
Hb (g/dL)	13.7±0.64	14.6±0.29	14.9±0.35	18.3±0.45 *
RBCs (10^6 µL)	7.1±0.62	7.5±0.24	7.8±0.27	9.8±0.35 *
PCV (%)	40.2±1.7	43.3±1.1	44.8±1.3	57.5±1.5 *
MCV (fL)	58.8±1.4	58.1±0.75	57.8±0.40	58.9±0.74
MCH (pg)	19.5±1.2	19.6±0.24	19.2±0.22	18.8±0.26
MCHC (g/dL)	33.3±1.7	33.9±0.34	33.2±0.23	31.9±0.20
PLT (10^3 µL)	650.5±83.2	789.7±53.1	813.7±103.2	903.6±77.1*
WBCs(10^3 µL)	9.0±1.4	9.1±1.1	9.4±10	6.1± 0.46*

Expressed as means ± STD * - significantly different from control (P< 0.05)

Table 3: The effect of repeated oral administration of the ethanolic extract of *X. americana* leaves for three weeks on some hematological parameters of experimental rats

There were no significant changes in the values of hemoglobin (Hb) concentration, red blood cell (RBCs) count and packed cell volume (PCV) in rats receiving 100 mg/kg (Group 2) and 200 mg/kg (Group 3) as compared to control rats (Group 1). However, there was a significant ($P < 0.05$) increase in these three hematological parameters (Hb, PCV and RBCs count) in Group 4 rats which received 400mg/Kg of the ethanolic extract. No significant changes in the values of red blood indices including mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) in all treated groups as compared to control. However, a significant ($P<0.05$) increase in platelet (PLT) count was further observed in Group 4 rats receiving 400mg/kg of ethanolic extract. A significant decrease in the white blood cell count (WBCs) was, on the other hand observed in Group 4 rats as compared to control.

Plasma Biochemical Findings:

No significant changes were observed in the mean values of total plasma protein, albumin, urea nitrogen, creatinine and the plasma enzyme activity of aspartate aminotransferase (AST) and alanine aminotransferase in experimental rats receiving repeated daily oral doses of the ethanolic extract of *X. americana* leaves at dose rates of 100 mg/kg body weight /day (Group 2), 200 mg/kg body weight /day (Group 3) and 400 mg/kg body weight / day (Group 4) for three weeks as compared to control group (Figures 1-6).

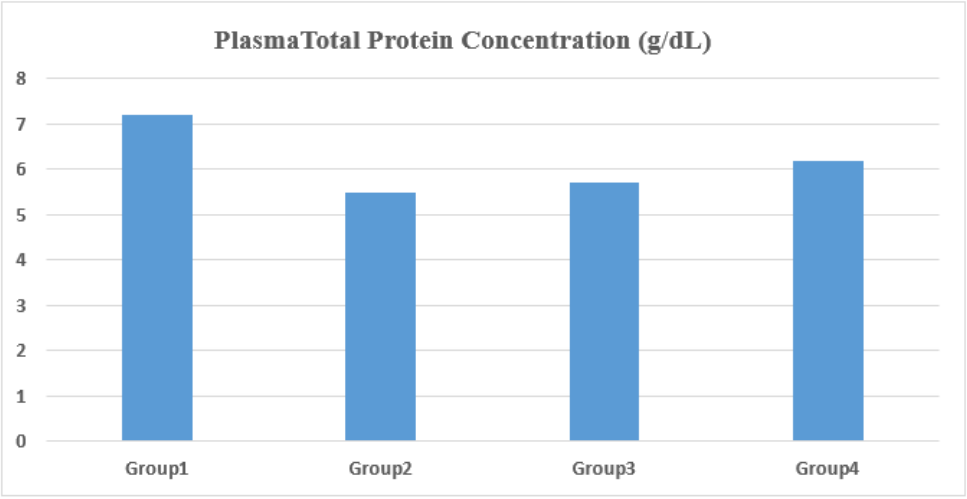

Figure 1. Plasma total protein concentration (g/dL) in control rats (Group1) and experimental rats administrated ethanolic extract of *X. americana* leaves at dose rates of 100 mg/kg/day (Group2), 200mg/kg/ day (Group3) and 400mg/kg/day (Group 4) for three weeks.

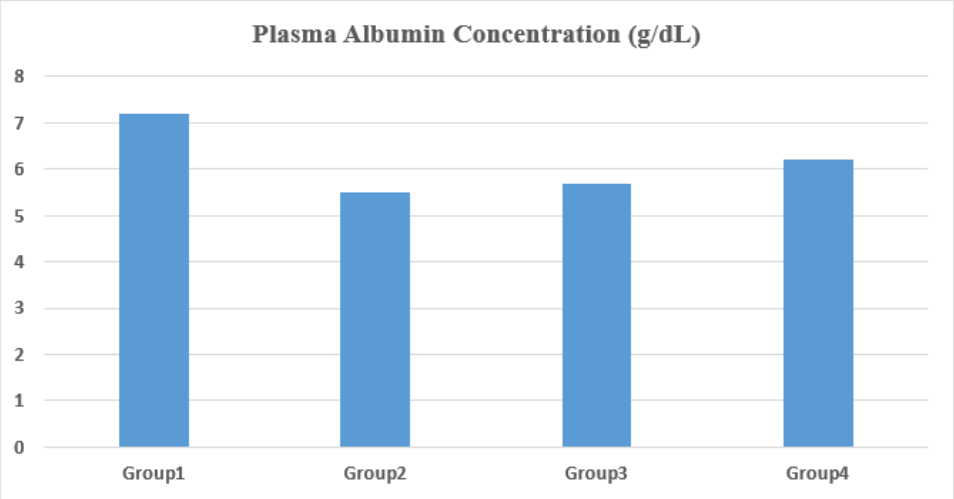

Figure 2. Plasma albumin concentration (g/dL) in control rats (Group1) and experimental rats administrated ethanolic extract of *X.americana* leaves at dose rates of 100 mg/kg/day (Group2), 200 mg/kg/ day (Group 3) and 400 mg/kg/day (Group 4) for three weeks

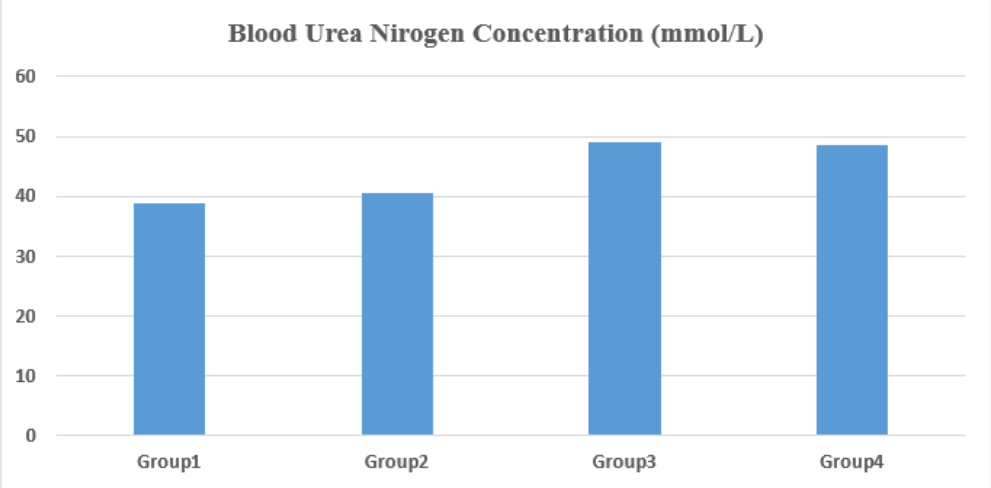

Figure 3. Blood urea nitrogen concentration (mmol/L) in control rats (Group1) and experimental rats administrated ethanolic extract of X. *americana* leaves at dose rates of 100 mg/kg/day (Group2), 200 mg/kg/ day (Group3) and 400 mg/kg/day (Group 4) for three weeks.

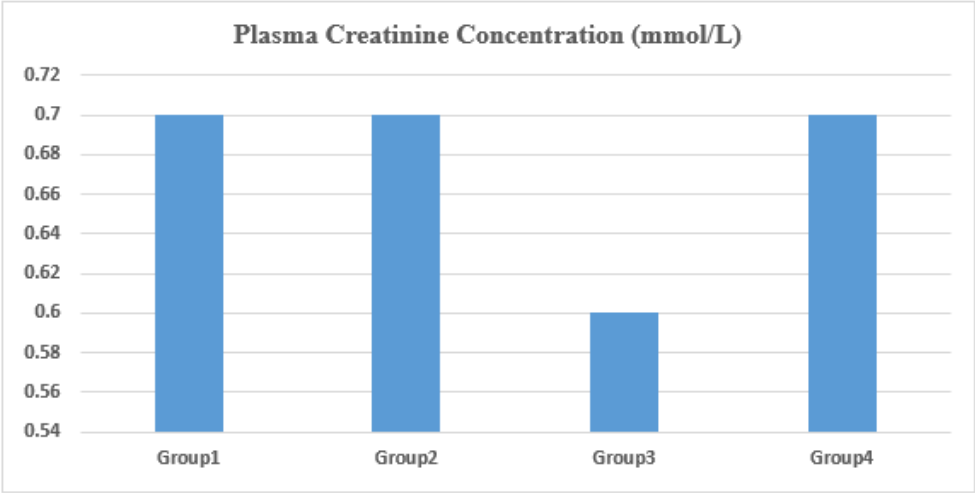

Figure 4. Plasma creatinine concentration (mmol/L) in control rats (Group1) and experimental rats administrated ethanolic extract of *X. americana* leaves at dose rates of 100 mg/kg/day (Group1), 200 mg/kg day (Group2) and 400 mg/kg/day (Group3) for three weeks

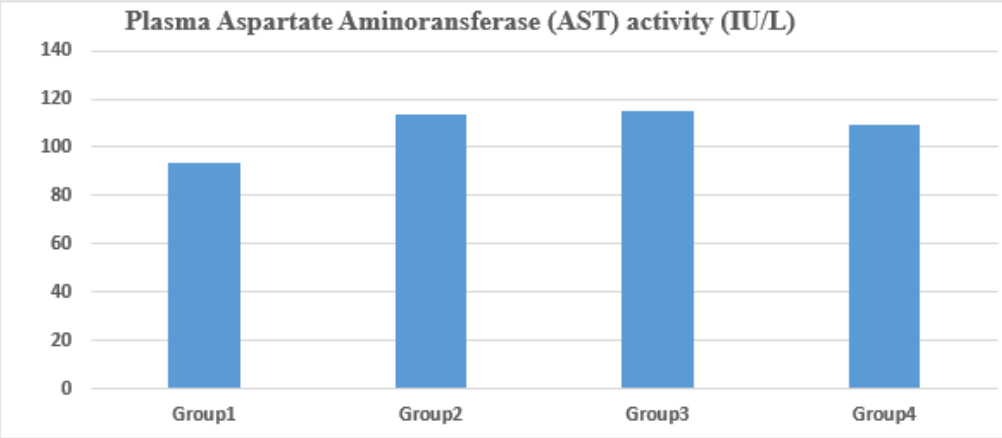

Figure 5. Plasma aspartate aminotransferase activity (IU/L) in control rats (Group1) and experimental rats administrated ethanolic extract of *X. americana* leaves at dose rates of 100 mg/kg/day (Group2), 200 mg/kg day (Group3) and 400 mg/kg/day (Group4) for three weeks

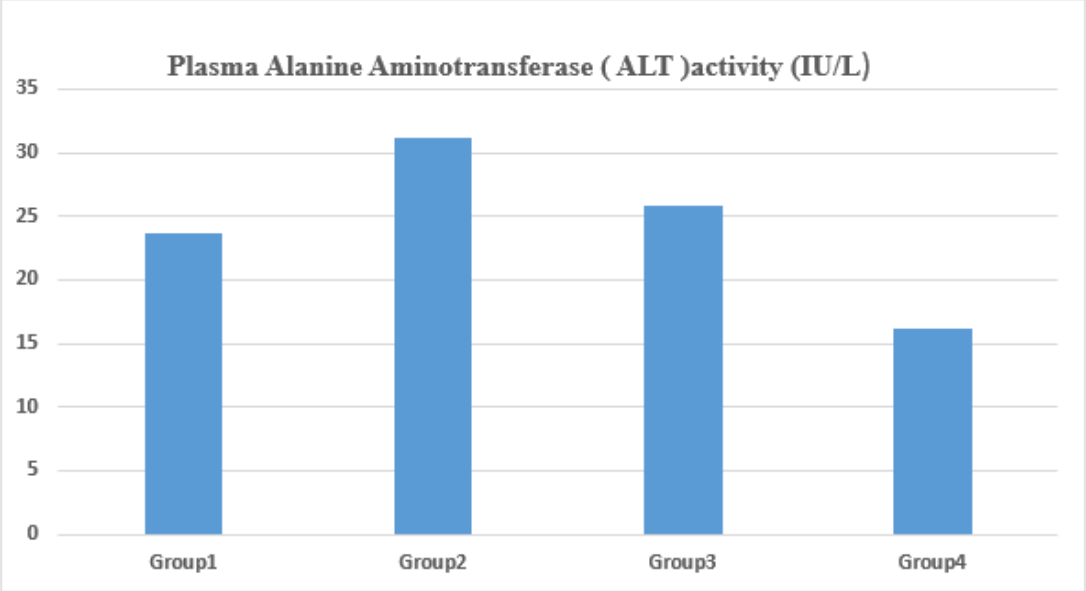

Figure 6. Plasma alanine aminotransferase activity (IU/L) in control rats (Group1) and experimental rats administrated ethanolic extract of *X. Americana* leaves at dose rates of 100 mg/kg/day (Group2), 200 mg/kg/ day (Group 3) and 400 mg/kg/day (Group 4) for three weeks.

Pathological Findings

No grossly detectable pathological lesions were observed in the body or in various visceral organs of control rats (Group 1) and in all experimental rats given repeated daily oral doses of the ethanolic extract of *X. americana* leaves for three weeks at dose rates of 100 mg/kg body weight (Group 2), 200 mg/kg body weight (Group 3) and 400 mg/kg body weight (Group 4). Also, no significant histopathological alterations were observed in the liver, kidney, heart, spleen and intestines of control and experimental groups. Figures 7, 8, 9. 10 and 11 show the absence of histopathological alterations in the liver, kidney, heart, spleen and intestines of Group 4 rats which received the highest dose (400 mg/kg/ day) of the ethanolic extract for three weeks.

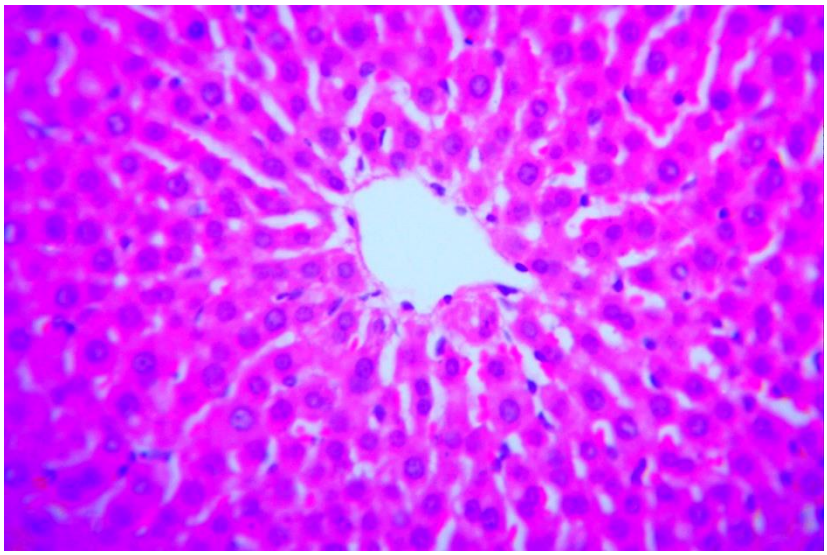

Figure 7: Liver of Group 4 rats receiving 400 mg/kg/day ethanolic extract of *X. americana* leaves for three weeks. No significant histopathological changes were observed (H&E X400)

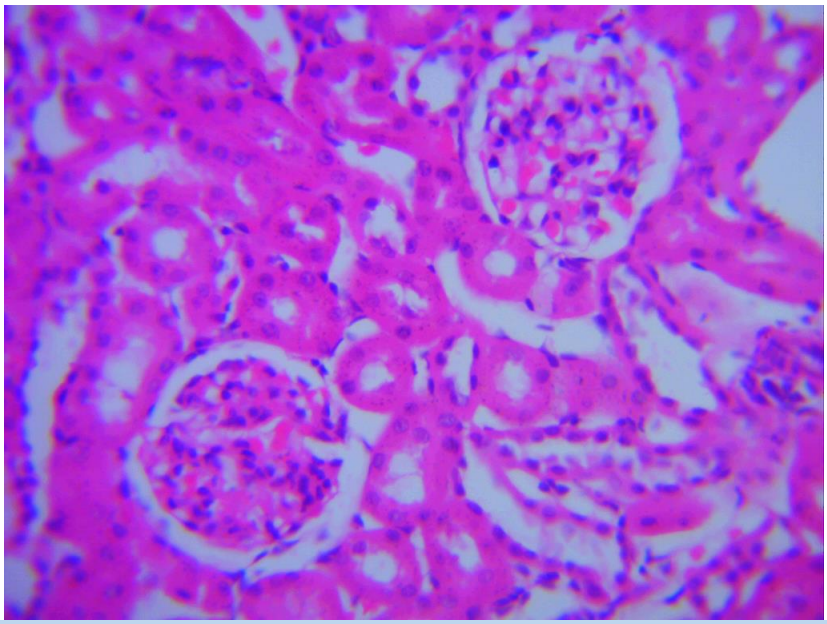

Figure 8. Kidney of Group 4 rats receiving 400 mg/kg/day ethanolic extract of *X. americana* leaves for three weeks. No significant histopathological changes were observed (H&E X400)

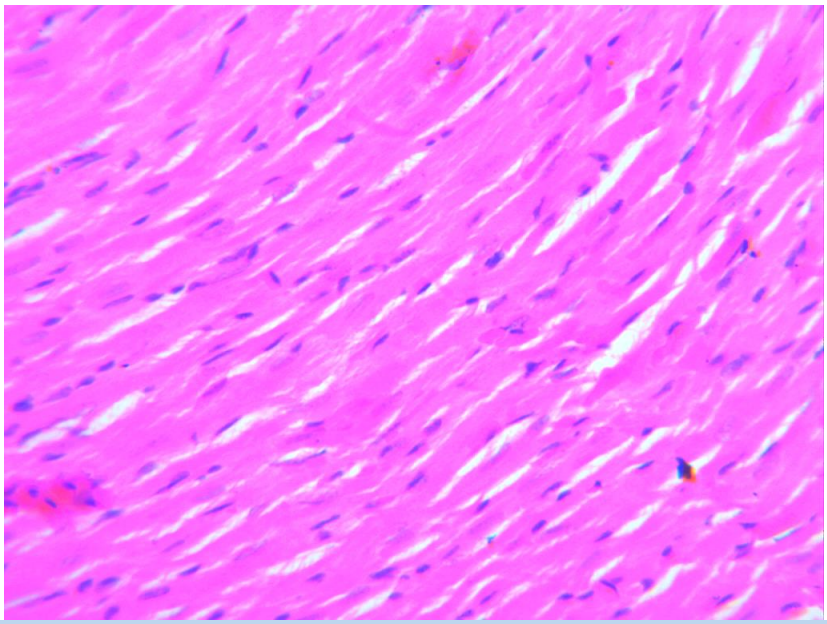

Figure 9. Heart of Group 4 rats receiving 400 mg/kg/day ethanolic extract of *X. americana* leaves for three weeks. No significant histopathological changes were observed (H&E X400)

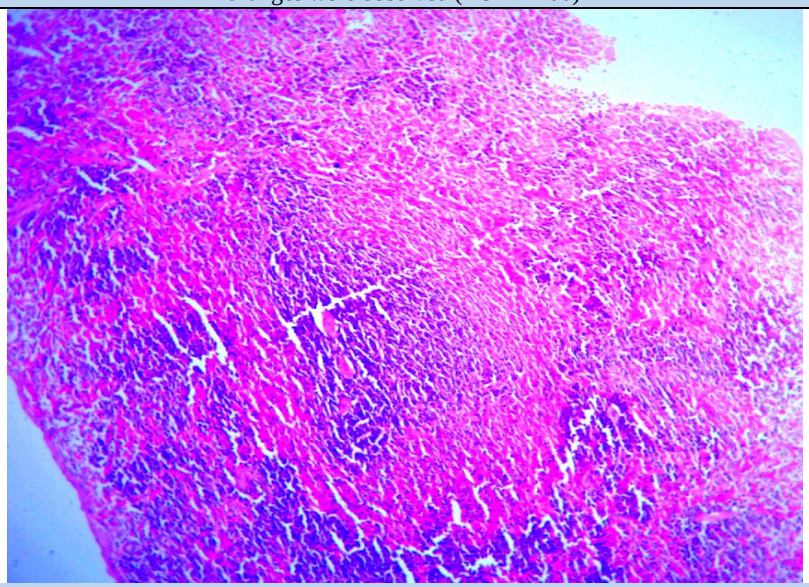

Figure 10. Spleen of Group 4 rats receiving 400 mg/kg/day ethanolic extract of *X.americana* leaves for three weeks. No significant histopathological changes were observed (H&E X100)

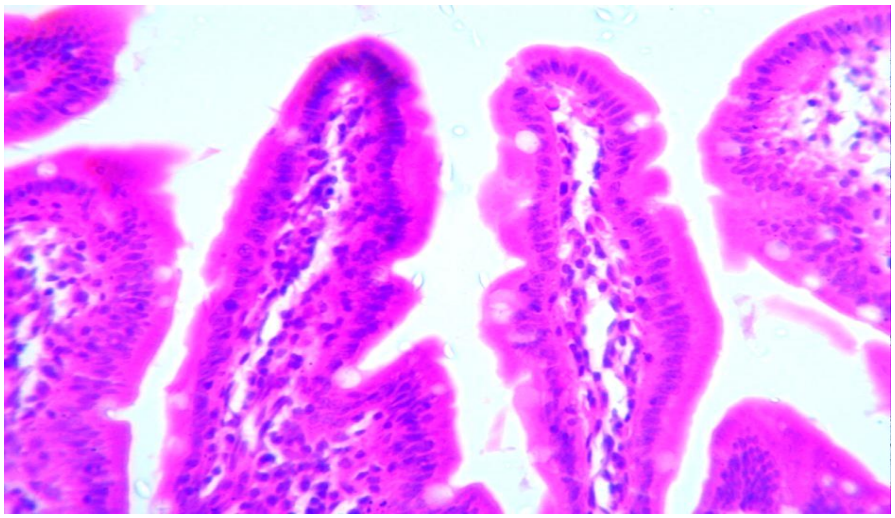

Figure 11. Small intestine of Group 4 rats receiving 400 mg/kg/day ethanolic extract of *X.americana* leaves for three weeks. No significant histopathological changes were observed (H&E X400)

Body Weight

The mean body weight of control and experimental rats receiving daily repeated oral doses of the ethanolic extract of *X. Americana* leaves for three weeks is shown in Figure 12.

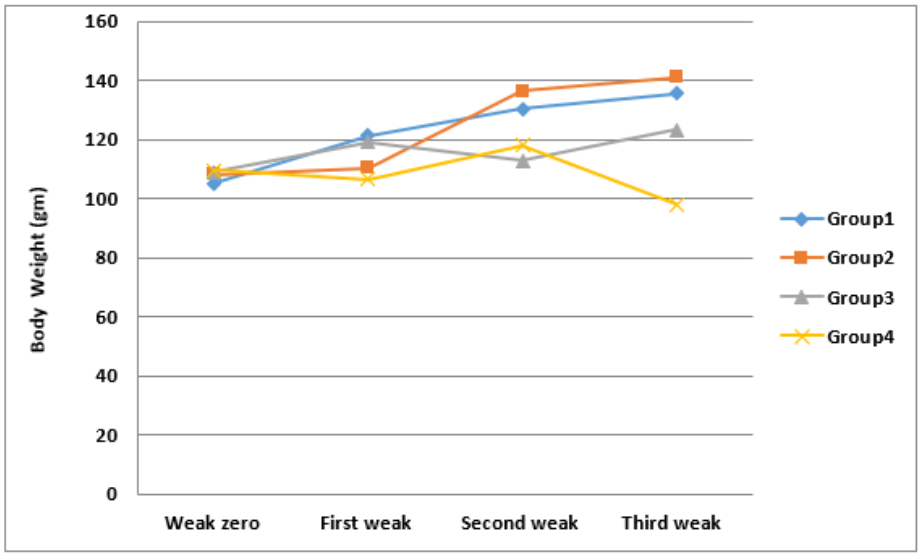

Figure 12: Mean body weight of control rats (Group 1) and experimental rats administered ethanolic extract of *X. americana* leaves at dose rates of 100 mg/kg/day (Group 2), 200 mg/kg/day (Group 3) and 400 mg/kg/day (Group 4) for three weeks.

There was a significant ($P<0.05$) increase in the mean body weight of experimental rats receiving 100 mg/kg/day (Group 2) by the end of the third week as compared to control rats (Group 1). No significant changes were observed in the mean body weight of experimental rats receiving 200 mg/kg/day (Group 3). However, a significant ($P<0.05$) decrease in the mean body weight was observed in experimental rats receiving 400 mg/kg/day (Group 4) by the end of the third week as compared to control rats.

Discussion

The results of the preliminary phytochemical analysis of the ethanolic extract of the dry leaves of *X. americana* in the present study revealed the presence of several biologically active ingredients including saponins, alkaloids, tannins, flavonoids, sterols and triterpenes. These biologically active ingredients have consistently been detected in aqueous, methanolic and ethanolic extracts of the stem bark, leaves and the root of the plant. [11,13,17,21,30]. It is well established that the beneficial pharmacological properties of the crude plant such as the analgesic, anti-inflammatory, antimicrobial, anticancer and antioxidant effects are mainly attributed to the presence of these biologically active ingredients [17, 21, 31].

The results of the toxicological evaluation of the plant revealed that the repeated daily oral administration of the ethanolic extract of the dry leaves of *X. americana* at dose rates of 100 mg, 200 mg and 400 mg /Kg body weight /day did not produce any adverse clinical effects on experimental rats when given for a period of three weeks. Similar studies have also demonstrated the absence of lethal or serious clinical effects on mice given the methanolic extract of the plant at single oral doses of 10, 100 and 1000 mg/Kg body weight [32]. Also, the repeated administration of

the methanolic extract of the stem bark of the plant did not produce adverse clinical changes in rats when the extract was given orally at dose rates of 250, 500 and 1000 mg/Kg body weight [33]. The results of the present work and the above mentioned reports therefore provide a good evidence of the wide margin of safety of the ethanolic extract of the dry leaves of *X.americana*.

The results of the present investigation also showed that the repeated administration of the ethanolic extract of the dry leaves of *X.americana* did not produce significant adverse effects on some hematological parameters including hemoglobin (Hb) concentration, red blood cell (RBCs) count, platelet count (PLT), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular (MCH) and mean corpuscular hemoglobin concentration (MCHC) in experimental rats when given as daily repeated oral doses of 100 and 200 mg/Kg body weight/ day for three weeks. These results are in agreement with previous findings indicating the absence of adverse effect of the methanolic or ethanolic extract of the stem bark or the dry leaves of *X.americana* on the major biochemical and hematological parameters of rats and mice [34,35]. On the other hand, a significant increase in Hb concentration, RBCs count, PCV, and PLT count was observed when the ethanolic extract was given at a dose level of 400 mg/Kg body weight. The increase in total erythrocyte count (RBCs) was probably due to an apparently stimulatory effect of the ethanolic extract of the dry leaves of *X.americana* on the hematopoietic function of the experimental rats. The possible stimulatory effect of *X.americana* on hematopoietic function explains the high efficacy of the plant in treatment of anemia associated with infectious diseases such as malaria and heavy parasitic infestation in human patients [36].

In the present investigation, the daily repeated oral administration of the ethanolic extract of the dry leaves of *X.americana* at dose rates of 100, 200 and 400 mg /Kg body weight for a period of three weeks did not produce significant effects in the plasma concentration of total protein, albumin, urea, creatinine and plasma activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in experimental rats. The lack of significant effect on those previously mentioned parameters demonstrates the negligible adverse effect of the plant on the liver and kidney structure and function. These findings are in agreement with those previously reported by Agyigra et al [33]. However, a contradicting report by Wurochekke et al [37] has, on the other hand, revealed a significant increase in the plasma AST activity with a significant reduction in the plasma protein concentration in albino rats receiving a total of 30 repeated oral doses of 240 mg /Kg body weight of the aqueous extract of the stem bark of *X.americana*. Further studies are therefore required to establish the precise effect of the plant on the liver and kidney function at different dose levels.

The results of the present investigation showed no significant gross or histopathological changes in the liver, kidney, heart, spleen and intestines of experimental groups of rats given repeated daily oral doses of 100, 200 and 400 mg /Kg body weight of the ethanolic extract of the dry leaves of *X. americana* for three weeks. The absence of significant histopathological changes in these organs is well correlated with the normal values of AST and ALT activity, total plasma protein, albumin, blood urea nitrogen and plasma creatinine concentration. The present results are therefore in agreement with previous findings indicating the relative safety of the plant with respect to an anticipated hepatorenal injury [32, 33].

Evaluation of the effect of the ethanolic extract of the dry leaves of *X.americana* on body weight performance showed a significant increase in the mean body weight of experimental rats receiving 100 mg/kg/day by the end of the third week. No significant changes were observed in the mean body weight of experimental rats receiving 200 mg/kg/day. The increase in the mean body weight of experimental rats receiving 100 mg/kg/day of the ethanolic extract was probably due to a stimulatory effect of the plant on the animal appetite and to the possible eradication of co-existing internal parasites by the repeated administration of the ethanolic extract of the plant. However, a significant decrease in the mean body weight of experimental rats was, on the other hand, observed when the ethanolic extract was given at 400 mg/Kg body weight. The reduction of the mean body weight of experimental rats receiving the higher dose of the ethanolic extract of the plant was probably due to the presence of tannins which were found to interfere with the gastrointestinal absorption of nutrients [38].

It is concluded from the present results that the tropical medicinal plant *X.americana* has an almost negligible adverse effect on rats when given as daily repeated doses up 400 mg/kg body weight /day for three weeks. The plant could therefore be safely used in folk medicine for treatment of various type of infectious and neoplastic diseases.

Acknowledgments

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Compliance with ethical standards

All procedures performed in the present investigation were in accordance with the ethical standards of the international and national guidelines for the care and use of animals.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Petrovsksa, B B (2012). Historical review of medicinal plants' usage. Pharmacognosy Reviews 6:1-5.
2. Kuete V (2014). Toxicological Survey of African Medicinal Plants. 1st Edn. Elsevier Inc.
3. Medeiros A C, Medeiros F (2018). Ximenia americana L.: Brazil. In "Medical and Aromatic Plants of South America") Springer (pp.477-486).
4. Calapai G (2008). European legislation on herbal medicines: a look into the future. Drug Safety 31: 428-431.
5. Anquez-Traxler C (2011). The legal and Regulatory Framework of Herbal Medicinal Products in the European Union: A Focus on the Traditional Herbal Medicines Category. Therapeutic Innovation and Regulatory Science 45: 15-23.
6. Ogunleye D S, Ibitoye S F (2003). Studies of Antimicrobial Activity and Chemical Constituents of Ximenia americana. Tropical Journal of Pharmaceutical Research 2:239-241.
7. Kerharo J, Adam J G (1974) The Traditional Senegalese Pharmacopeia. Medicinal Herbs and Poisons. Vigot brothers, Paris, France. P.1007.
8. Tapsoba H, Deschamps J (2006). Use of medicinal plants for the treatment of oral diseases in Burkina Faso. Journal of Ethnopharmacology 104:68-78.
9. Magassouba E B, Diallo A M, Kouyate F, Mara O, et al, (2007). Ethnobotanical survey and antibacterial activity of some plants used in Guinean traditional medicine. Journal of Ethnopharmacology 114: 44 - 53.
10. Freiburghaus, F., Kaminsky, R.., Mayunga, H. H. N and Brun, R. (1996). Evaluation of African medicinal plants

for their in vitro trypanocidal activity. Journal of Ethnopharmacology. 55: 1-11

11. Nwodo, N.J., Ibezim, A., Ntie-Kang, F., Adikwu, M.U. and Mbah, C.J. (2015). Anti-Trypanosomal Activity of Nigerian Plants and Their Constituents. Molecules. 20:7750-7771.
12. Koné W M, Kamanzi Atindehou K, Terreaux C, Hostettmann K, Traoré D, Dosso M (2004). Traditional medicine in North Côte-d'Ivoire:screening of 50 medicinal plants for antibacterial activity. Journal of Ethnopharmacology. 93, 43-49.
13. Kumar-Roine S, Matsui M , Reybier K, Darius H T, Chinain M, et. al., (2009). Ability of certain plant extracts traditionally used to treat ciguatera fish poisoning to inhibit nitric oxide production in RAW264.7 macrophages. Journal of Ethnopharmacology 123: 369-377.
14. Urso, V. Signorini, M.A. and Bruschi P. (2013). Survey of the ethnobotanical uses of Ximenia americana L. (mumpeke) among rural communities in South Angola. Journal of Medical Plant Research 7: 7-18.
15. Arora, D, Kaur, I (1999). Antimicrobial activity of spices. International Journal of Antimicrobial Agents 12:257-262.
16. Geyid A, Abebe D, Debella A, Makonnen Z, Aberra F, et. al., (2005). Screening of some medicinal plants of Ethiopia for their anti-microbial properties and chemical profiles. Journal of Ethnopharmacology 97: 421-427.
17. James D B, Abu E A, Wurochekke A U, Orgi G N (2007). Phytochemical and Antimicrobial Investigation of the aqueous and methanolic extracts of Ximenia Americana. Journal of Medical Sciences 7: 284-288.
18. Doka I G, Yagi S M (2009). Ethnobotanical Survey of Medicinal Plants in West Kordofan (Western Sudan) Ethnobotanical Leaflets 13: 1409-1416.
19. EL-Kamali H H (2009). Medicinal Plants in East and Central Africa: Challenges and Constraints, in "Ethnobotanical Leaflets 13: 364-69.
20. Issa T O, Mohamed Y S, Yagi S R, Ahmed R H, Najeeb T M, Makhawi A M, Khider T O (2018). Ethnobotanical investigation on medicinal plants in Algoz area (South Kordofan), Sudan. *Journal of Ethnobiology and Ethnomedicine*, 14: 31
21. Sharief T M, Bashier R S M, Haroon M I (2022). Phytochemical Evaluation and Uses of Ximenia americana L in Central Darfur. International Journal of Current Microbiology and Applied Sciences 11:353-360.
22. Sukhdev S H (2008) An Overview of Extraction Techniques for Medicinal and Aromatic Plants. In: Sukhdev, S.H., Suman, P.S.K., Gennaro, L. and Dev, D.R., Eds., Extraction Technologies for Medicinal and Aromatic Plants. United Nations Industrial Development Organization and the International Centre for Science and High Technology, Trieste, Italy, 25-54.
23. Trease G E, Evans W C (1983).Textbook of Pharmacognosy, 12th Edn. Bailliere Tindall, London.
24. Weichselbaum T E (1946). An accurate and rapid method for the determination of proteins in small amounts of blood serum and plasma. American Journal of Clinical Pathology 10: 40 – 49.
25. Northam B E, Widdowson G M (1967). Determination of serum albumin by auto analyzer using bromocresol green. Technical bulletin No.11 Association of Clinical Biochemists. London.
26. Fawcett J K, Scout J E (1960). A rapid and precise method for the determination of urea. Journal of Clinical Pathology 13:156 -159.
27. Bartels H, Böhmer M (1973). A kinetic method for measurement of creatinine in serum. Med Lab (Stuttg) 26:209- 215.
28. Reitman S, Frankel A (1957) A Colorimetric Method for the Determination of Serum Glutamic Oxalacetic and Glutamic Pyruvic Transaminases. American Journal of Clinical Pathology 28:56-63.
29. Bancoft J D, Gamble M (2007). Theory and Practice of Histological Techniques. 6th edn. Churchill Livingston, Edinburgh.
30. Araújo M R S , Da Costa J C, Assunção I N, Nogueira I, Dantas F, Veras L, Costa-Lotufo L V, Monte F J Q (2008). Chemical Constituents of Ximenia americana. Natural Product Communications 3: 857- 860.
31. Soro TY, Zahoui O S, Néné-bi AS, Traoré F (2015). Antipyretic activity of the fractions of aqueous extract from Ximenia americana (Linnaeus Olacaceae). International of Pharmacology and Toxicology 5:104 - 108.
32. Maika V, Kobo P I, Adaudi A O (2008). Acute toxicity studies of aqueous stem bark extract of Ximenia americana. African Journal of Biotechnology 7:1600-1603.
33. Agyigra I, Ejiofor J.I.,Magaji M J (2017). Acute and subchronic toxicity evaluation of methanol stem-bark extract of Ximenia americana Linn (Olacaceae) in Wistar rats. Bulletin of Faculty of Pharmacy Cairo University 55:263- 267.
34. Togbossi L A, Lawson-Evi1 P, Atchou1 N K, Motto1 EA, Diallo A, EkluGadegbeku1 K, Aklikokou K (2022). In vivo assessment of acute and subchronic toxicity of hydroethanolic extract of Ximenia americana L. (Olacaceae) stem bark. Journal of Drug Delivery and Therapeutics 12:81-86.
35. James D B, Owolabi AO, Ibiyeye H, J. Magaji J, Ikugiy YA (2008). Assessment of the hepatic effects, hematological effect and some phytochemical constituents of Ximenia americana (Leaves, stem and root) extract. African Journal of Biotechnology 7: 4274-4278.
36. Peter E L, Rumisha S F, Mashoto KO, Malebo M M (2014). Ethno-medicinal Knowledge and Plants Traditionally Used to Treat Anemia in Tanzania: A cross Sectional Survey. Journal of Ethnopharmacology 154: 767 – 773.
37. Wurochekke A U, Anthony A E, Obidah W (2008). Biochemical effects on the liver and kidney of rats administered aqueous stem bark extract of Xemenia americana. African Journal of Biotechnology 7: 2777-2780.
38. Kumar R, Singh M (1984) Tannins: Their Adverse Role in Ruminant Nutrition. Journal of Agricultural and Food Chemistry 32: 447-453.

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