African Journal of
Sciences and Traditional Medicine

ISSN : 3434-6031

Index: Harvard, Boston, Sydney University, Dimensions, Lens, ResearchGet Scilit, Semantic, Google Scholar, Base etc

https://doi.org/10.58578/AJSTM.v1i2.3476

Biorenal Effects of the Polyherbal (*Andrographis paniculata, Annona muricata, Zingiber officinale*) Aqueous Extract on Wistar Rats

Benjamin Ogunma Gabriel[1], Ehonwa Lisa Osawese[2], Emmanuel Ola Oshomoh[3]
University of Benin, Edo State, Nigeria
alexthemain@yahoo.com; alexthemain076@gmail.com

Article Info:

Submitted:	Revised:	Accepted:	Published:
Aug 20, 2024	Sep 1, 2024	Sep 15, 2024	Sep 21, 2024

Abstract

There has been a reliance on medicinal plant parts and their extracts for the prevention and treatment of diseases throughout history. Toxicological studies have now shown concern on the unavailability of standard dosage for the treatment of these substances that causes for concern. This study evaluated the bio-renal safety of the polyherbal aqueous extract of in Wistar rats. The aqueous extracts were obtained using standard methods. A total of 25 adult rats were used and administered to the tested groups for 28 days. Kidney function test was carried out together with histopathological evaluations of the kidneys of the rats. The results obtained showed that urea, creatinine, Na+, K+, Cl- and HCO- concentrations across 25-57 mg/dl, 0.1-0.8 mg/dl, 134-142 µmol/l, 4.4-4.9 µmol/l, 96-103 µmol/l and 21-28 µmol/l, had no significant difference at graded doses of the treatment groups respectively. These results were in the normal range when compared with the control. The histopathological study of the kidney tissues showed normal architectural structures with visible renal corpuscles and distinct tubules. In conclusion, the polyherbal aqueous extract had no adverse effects across the tested animals at graded doses. However, further research is recommended for drug evaluation.

Keywords: Biorenal, Polyherbal, *Andrographis paniculata, Annona muricata, Zingiber officinale*, Wistar Rats

INTRODUCTION

Herbal preparations and decoctions are dispensed and consumed without and regulation of the quantities which are consumed by the users. The efficacy and safety of these extracts are not accompanied by quality control measures and are generally not backed by scientific evidence (Anyanwu et al., 2017; Khaleel et al., 2021). The kidneys are important organs in the body which function in the removal of certain waste products of metabolism from the blood of living organisms. They are one of the organs which are heavily affected when toxic compounds accumulate in the body and such exposures lead to injuries or even death of kidney tissues (Habib et al., 2022). The consumption of unregulated amounts of herbal preparations over long time periods may induce toxicity and affect the organs of the body including the kidneys because of the bioactive constituents of these plants such as alkaloids (Imo et al., 2019).

The stems and leaves of *Andrographis paniculata* as the main bioactive substance known as andrographolide. The concentration of andrographolide is highest in the leaves (2.39%) and lowest in the seeds (0.58%) (Dai et al., 2019). *A. muricata* have virucidal properties (Coria-Tellez et al., 2018). Coagulation, inflammation, proliferation, and maturation are the four phases of wound healing, which are essential for healing due to their function in cell proliferation during the inflammatory phase (Moghadamtousi et al., 2015). Along with this anti-inflammatory effect, leukocyte migration and exudate volume were decreased. *Zingiber officinale* was first used as a spice. Up to 3% of the essential oil that gives ginger its distinctive scent may be found in ginger. Ginger is consumed often and is a well-known treatment for digestive issues in India and other nations with hot, humid climates (Wakchure and Ganguly, 2018).

MATERIALS AND METHODS

Plant Collection and Identification

The three plant species selected for use in this study (*Annona muricata, Andrographis paniculata* and *Zingiber officinale*) were procured from Benin City, Edo state. They were identified in the Department of Plant Biology and Biotechnology with Voucher number (UBH-A2714, UBH-A2800, UBH-Z0118).

Sample Preparation

Fresh leaves from the plant samples were cleaned in clean water, cut into pieces, and dried in the shade for fourteen (14) days. It was then dried in the oven for a further 24 hours at

45°C. To create a polyherbal blend, the powdered leaf samples were individually weighed using different weight units. Distilled water was then used to extract the combination for 72 hours while intermittently swirling and shaking. It was filtered, and the filtrate was then condensed into semi-solid using crucibles over a water bath. Percentage yield was calculated using the formula below

Experimental animals/ Design

At the Animal House, Department of Biochemistry, University of Benin, Nigeria, twenty-five (25) adult Wistar rats were raised. They were housed in spotless cages at ambient temperature. The rats had unrestricted access to conventional rat food and water for the duration of the experiment. They were weighed before the study began and once a week afterwards for the duration of the trial, with the findings recorded to the nearest whole number on a digital scale calibrated in grams. The procedures followed were in line with manuals for the handling and using of experimental animals with ethical number of LS22015.

At the end of the exposure period, the rats were sacrificed using cotton wools soaked in chloroform. The cotton wools were placed in a container with the rats and induced them to sleep upon which all the blood settled in their stomach. The stomachs were then cut open with a scissors and a syringe was used to collect the blood into bottles containing anticoagulants which prevented the blood from clotting. The bottles were kept on ice. The kidneys of the rats were then extracted from each group and preserved using formalin.

Renal function test

Assay for urea

This test exploits the hydrolysis of urea into ammonia in urease enzyme presence. 100 µls of reagent 1 was added to 10 µl of serum sample in a test tube. 100 µl solution of the reagent 1 was added into 10 µls water as blank. Solutions in test tubes were thoroughly mixed for incubation in 10 minutes at 37°C. Similarly, 2.5 mls of reagents 2 and 3 were added into test tubes. Solutions in test tubes were properly mixed for incubation in 10 minutes at 37°C. Sample absorbances and standard against blank with 546 nm wavelength. Urea concentration calculation as thus:

Urea concentration (mg/dl) = Absorbance of sample/ Absorbance of standard x 80.

Assay for creatinine

This test exploits the reaction of creatinine present in alkaline solution having picric acid producing complex coloration. Quantity of complex colour synthesized directly relative to creatinine concentration. The sample of macro and semi micro of 0.2 ml was added to test tube. 0.2 ml of standard macro and 0.1 ml of semi micro were added to the standard solution test tube. Two (2) ml of standard macro, 1 ml of semi micro, 2 mls of sample macro and 1 ml of semi micro were added to the working reagent test tube. The solutions in test tubes were properly mixed. Absorbance's of samples and standard being read using 492 nm. Creatinine values were calculated as thus:

Creatinine level unit (mg/dl) = Absorbance of sample/Absorbance of standard x 2.

Assay for electrolytes (Sodium, chloride, bicarbonate and potassium)

The assay for bicarbonate exploits the reaction between bicarbonate ions with dilute hydrochloric acid to yield carbon dioxide. The excess acid is titrated with dilute sodium hydroxide using phenol red as indicator. Solution of 0.01 N HCl was added to 200 µls of serum sample. The solution was mixed and 1 drop of phenol red indicator added. Mixture was titrated using 0.01 N sodium hydroxide to acquire brick red colour which serves as endpoint (Van Skye and Neil, 1924). Bicarbonate was calculated as thus:

Bicarbonate (µmol/l) = 50 – Titre 5

Titre = Endpoint x 100.

The assay for chloride exploits the formation of chloride precipitate in a sample using mercuric nitrate. When chloride is titrated with standard solution of mercuric ion, undissociated but stable mercuric chloride is formed. The excess mercuric chloride nitrate reacts with diphenylcarbazone to produce a violet coloration. 2 mls deionized water added to 200 µls of serum sample. This solution was properly mixed; 3 drops of diphenylcarbazone indicator and 1 drop of nitric acid were added. Mixture was titrated in mercuric nitrate to give violet endpoint. The same procedure was repeated for chloride standard solution (Andjelkovic et al*.,* 2019). Chloride was calculated below:

Chloride (µmol /l) = Titre of the sample/Titre of the standard x 100.

The assay method for sodium and potassium entails the injection of solutions containing these elements in flame leaving solid salt, which dissociates to neutral ground state. The atoms become excited in the flame, thus moving to a higher energy state. The excited atoms then fall back to ground state emitting light of characteristic wavelength (590 nm for sodium and 770 nm for potassium). The light passes through a suitable filter onto a photosensitive element and the amount of current measured was proportional to the amount of sodium and potassium present in the serum sample (Mutar et al., 2020)

Histopathological analyses

Kidneys of the rats were fixed in neutral buffered formalin. Affixed organs were utterly dehydrated with 99.9% ethanol along with 70% ethanol, 96% ethanol and washed using distilled water. 4 micrometre sections were prepared and stained in haematoxylin-eosin dye. Stained tissues were viewed at x400 magnification using an optical photomicroscope (Leica MC170 HD, Leica Biosystems, Germany) (Drury and Wallington, 2013).

Statistical analysis

Results were analysed with Graph Prism version 6. Data was presented as Mean ± SEM, and statistical significance were determined using One-way ANOVA, followed by Dunnett's test. Where $p<0.05$, results were considered to be statistically significant.

RESULTS

Kidney Function Tests

The results obtained from the urea level in kidney function test across graded doses of the extract elicited a significant increase at 200, 400 and 800 mg/kg of the polyherbal aqueous extract when compared with the untreated control, though all within the normal range of urea level. This as shown in Table 1

Table 1: Effects of poly-herbal leaf aqueous extract on Urea in Wistar rats

Groups	Doses (mg/kg)	Urea (mg/dl)
Control	0.5 ml	26.33 ± 0.88^{a}
PAE	200	38.67 ± 4.17^{b}
PAE	400	41.33 ± 6.89^{b}
PAE	800	43.00 ± 7.10^{b}

P -value > 0.05, same superscript is not statistically significant. Key: PAE (poly-herbal aqueous extract)

The results obtained from the creatinine level in kidney function test across graded doses of the extract elicited a significant reduction at 200, 400 and 800 mg/kg of the polyherbal aqueous extract, specifically at 200 mg/kg when compared with the untreated control, though all within the normal range of creatinine level. This as shown in Figure 1

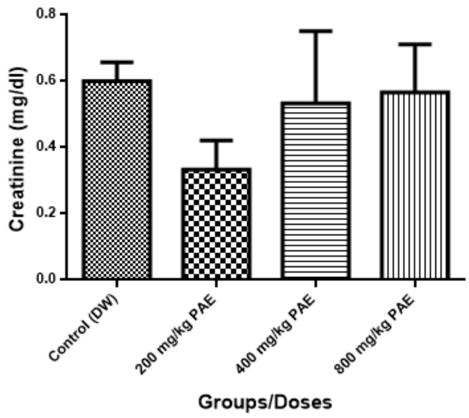

Figure 1: Effects of poly-herbal aqueous extract on creatinine level in Wistar rats.

Key: PAE (poly-herbal aqueous extract), DW (distilled water)

The results obtained from the sodium level in kidney function test across graded doses of the extract displayed no significant difference at 200, 400 and 800 mg/kg of the polyherbal aqueous extract but with slight decrease across the doses when compared with the untreated control, though all within the normal range of sodium level. This as shown in Table 2.

Table 2: Effects of polyherbal aqueous extract on sodium level in Wistar rats

Groups	Doses (mg/kg)	Sodium (mg/dl)
Control	0.5 ml	140.30 ± 0.88[a]
PAE	200	137.00 ± 1.00[a]
PAE	400	139.370 ± 0.88[a]
PAE	800	136.30 ± 1.45[a]

P -value > 0.05, all superscript a are not statistically significant. **Key:** PAE (poly-herbal aqueous extract)

The results obtained from the potassium level in kidney function test across graded doses of the extract exhibited a slight significant increase at 200, 400 and 800 mg/kg of the polyherbal aqueous extract, specifically at 200 mg/kg doses when compared with the untreated control, though all within normal range of potassium level. This as shown in Figure 2.

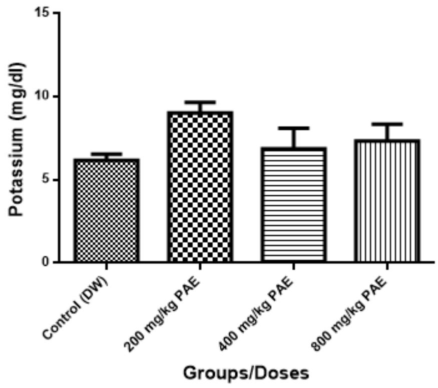

Figure 2: Effects of polyherbal aqueous extract on potassium level in Wistar rats.

Key: PAE (polyherbal aqueous extract), DW (distilled water)

The results obtained from the chloride level in kidney function test across graded doses of the extract displayed no significant difference at 200, 400 and 800 mg/kg of the polyherbal aqueous extract when compared with the untreated control, though all within the normal range of chloride level (Table 3).

Table 3: Effects of polyherbal aqueous extract on chloride in Wistar rats

Groups	Doses (mg/kg)	Chloride (mg/dl)
Control	0.5 ml	101.30 ± 0.88^{a}
PAE	200	99.67 ± 0.88^{a}
PAE	400	99.33 ± 1.67^{a}
PAE	800	100.30 ± 0.33^{a}

P -value > 0.05, all superscript a is not statistically significant. **Key:** PAE (polyherbal aqueous extract)

The results obtained from the bicarbonate level in kidney function test across graded doses of the extract displayed no significant difference at 200, 400 and 800 mg/kg of the polyherbal aqueous extract except at 400 mg/kg that had a slight significant increase across the doses when compared with the untreated control, though all within the normal range of bicarbonate level. This as shown in Figure 3.

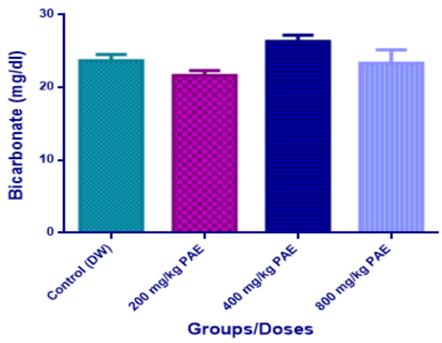

Figure 3: Effects of polyherbal aqueous extract on bicarbonate in Wistar rats.

Key: PAE (polyherbal aqueous extract), DW(distilled water)

The results of the histopathological alterations of the kidneys of the rats as shown in Plate 1. The kidney tissues of the untreated rats revealed a visible renal corpuscle with interstitial space and tubules. 200 mg/kg of the extract showed a visible renal corpuscle, surrounded by mild inflammatory cells, while the tubules present are distinct. 400 mg/kg of the extract renal corpuscles elicited a visible and well distinct tubule. 800 mg/kg of the extract had visible renal corpuscles surrounded by mild inflammatory cells, however, the tubules in the kidney tissues were not so distinct.

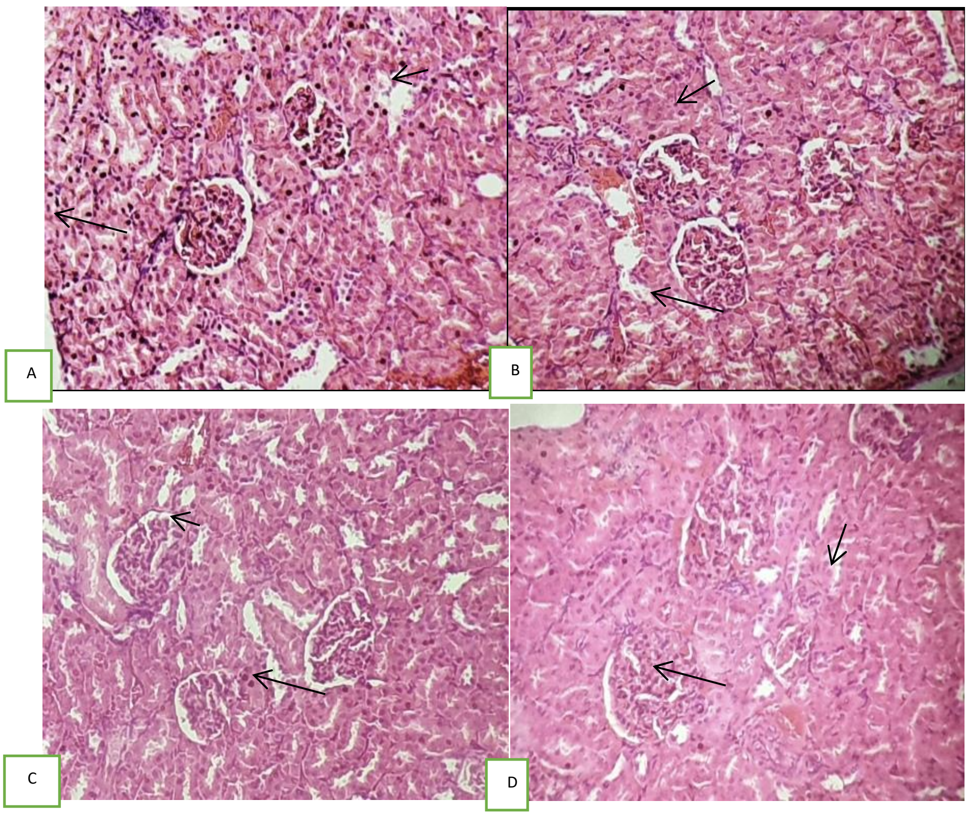

Plate 1: Effect of the polyherbal aqueous extract on renal cells in Wistar rats

A. Untreated control: Kidney reveals visible renal corpuscle (long arrow) and interstitial space (short arrow) and tubules.

B. 200 mg/kg aqueous extract: Kidney reveals visible renal corpuscle (long arrow) with mild inflammatory cells surrounding it (short arrow) the tubules appears distinct.

C. 400 mg/kg aqueous extract: Kidney reveals visible large renal corpuscle (long arrow) the tubules appear distinct (short arrow).

D. 800 mg/kg aqueous extract: Kidney reveals visible renal corpuscle (long arrow) with mild inflammatory cells surrounding it (short arrow) the tubules appears not so distinct.

DISCUSSION

The research into and use of medicinal plants has served mankind for generations in the prevention and treatment of a wide range of ailments. However, the use of these medicinal plants and their extract posed threat to health and well-being of consumers because of the lack of standardisation for dosages to be used (Anyanwu et al., 2017). These plants and their extracts may be consumed in quantities which may cause no harmful effect on various organs of the body particularly in renal tissues, which is responsible for drug either active or inactive form clearance (Khaleel et al., 2021). Renal biomarkers investigated in this study (Tables and Figures 1-3) revealed that the concentrations of urea at graded doses of the extract had a slight significant increase (25 – 57 mg/dl) when compared with the control. The significant level of the urea obtained in this present study far exceeded the values reported by Saka et al. (2012) using *Aloe vera* extract on rats and the urea concentrations obtained where 3.5 to 4.0 mg/dl. Imo et al. (2021) also reported the significant increase in the urea level (3.43 to 4.77 mg/dl) in kidneys of rats exposed to *Piper guineense* extracts. Based on the slight elevation of the urea level, where implicated in a decrease in the rate of glomerular filtration thereby causing accumulation of the toxic waste to kidney enzymes (Bazzano et al., 2015). Creatinine is one of the enzymes present in the kidney that checked mate its physiological functions in a healthy kidney due to the ease in measuring its concentration. Creatinine concentrations across the graded doses of the polyherbal aqueous extract had no significant increase (0.1 - 0.8 mg/dl) when compared with the untreated control. The levels of creatinine reported by a similar study of Agbafor et al. (2015) whose creatinine concentrations (0.23 to 0.78 mg/dl) increased when exposure of rats due to the administered *Ageratum conyzoides* extract. In the same vein, Khaleel et al.

(2021) reported a significant decreased in creatinine levels (1 mg/dl) when treated with *Ziziphus spina-christi* extract. Sodium, potassium, chloride and bicarbonate electrolytes were also investigated and no significant difference across the graded doses of the aqueous extract (134 - 142 µmol/l; 4.4 - 9.8 µmol/l; 96 - 103 µmol/l and 21 - 28 µmol/l), respectively where observed. Imo et al. (2019) investigation showed that the ions in kidney cells when pre-exposed to *Datura metel* extracts had no significant difference compared with the control across sodium, potassium and bicarbonate concentrations (137.75 - 138.90 mg/dl; 4.43 - 4.83 mg/dl and 24.50 - 27.00 mg/dl) respectively, while the concentration of chloride (104.75 - 107.75 mg/dl) had a slight increase when contrasted with the control. Also, similar results were reported by Isah et al. (2018) upon exposure of rats to *Senna occidentalis* extract on electrolytes concentration.

The histopathological properties of the extract at graded doses (Plate 1) revealed a normal architechtural appearance of the kidney with a visible renal corpuscles, interstitial spaces and tubules, also, with a distinct tubule when compared with the control. This indicated that the extract triggered no damaging effect on kidney cells of the rats. This is similar with the renal features reported by Jacques et al. (2016) and Isah et al. (2018) on rats pre-exposed to *Tephrosia vogelii* with no adverse effect on the kidney cells. However, a normal renal corpuscle indicated a visible and distinct tubule, with no evidence of mild inflammatory cells around the corpuscle as displayed in this present study. These changes adhere to the findings of Imo et al. (2019) whose work showed no significant increase in the activity of the kidney upon exposure to selected plant extracts.

CONCLUSION

This study was carried out to determine the impacts of the plant materials on the effect of normal renal functioning and possible histopathological changes of kidney tissues as revealed from this study. The plant scientific validation adhered to their ethnomedicinal report of therapeutic potential.

Recommendation

Further findings as regards renoprotective effect in novel drug development. The plant should be considered a traditional drug for health remedy. The extract elicited therapeutic effect boosting liver cells

Acknowledgment

We the authors appreciate the effort of Mr. Dalet and Dr. Kelvin and Prof Eze for the biochemical analysis and histopathological evaluation in University of Benin teaching Hospital, Department of Anatomy University of Benin, and Department of Pharmacology, University of Benin, for the Laboratory equipment used.

Competing Interests

Authors have declared that no competing interests exist.

REFERENCES

Agbafor, K.N., Engwa, G.A., Ude, C.M., Obiudu, I.K., Festus, B.O. (2015). The effect of aqueous leaf extract of *Ageratum conyzoides* on blood glucose, creatinine and calcium ion levels in albino rats. Journal of Pharmaceutical, Chemical and Biological Sciences, 3(3): 408-415.

Ahmed, K., Shaheen, G., Asif, H.M. (2011). *Zingiber officinale* Roscoe (pharmacological activity). Journal of Medicinal Plants Research, 5(3): 344-348.

Andjelkovic, M., Buha D.A., Antonijevic, E., Antonijevic, B., Stanic, M. et al. (2019). Toxic effect of acute cadmium and lead exposure in rat blood, liver, and kidney. International journal of environmental research and public health, 16(2): 274-283.

Anyanwu, S., Inyang, I.J., Asemota, E.A., Obioma, O.O., Okpokam, D.C., Agu, V.O. (2017). Effect of ethanolic extract of *Chromolaena odorata* on the kidneys and intestines of healthy albino rats. Integrative Medicine Research, 6(3): 292-299.

Ayoade, W.G., Amoo, I.A., Lajide, L., Ajayi, M.G. (2022). Phytochemicals and antioxidant potential of ginger (Zingiber officinale) and garlic (Allium sativum) extracts. GSC Biological and Pharmaceutical Sciences, 19(1): 226-234.

Bazzano, T., Restel, T.I., Porfirio, L.C., Souza, A.S.D., Silva, I.S. (2015). Renal biomarkers of male and female Wistar rats (Rattus norvegicus) undergoing renal ischemia and reperfusion. Acta cirurgica brasileira, 30: 277-288.

D'souza, M.R., Athoibi, S., Prabha, S. (2020). Pharmacognostical Investigation of Andrographis paniculata (Green Chiretta) and Crystallization of the Bioactive component Andrographolide. International Journal of PharmTech Research, 13(2): 40 - 50.

Dai, Y., Chen, S.R., Chai, L., Zhao, J., Wang, Y., Wang, Y. (2019). Overview of pharmacological activities of Andrographis paniculata and its major compound andrographolide. Critical reviews in food science and nutrition, 59(1): S17-S29.

Gajalakshmi, S., Vijayalakshmi, S., Devi, R.V., 2012. Phytochemical and pharmacological properties of Annona muricata: a review. International Journal of Pharmacy and Pharmaceutical Sciences, 4(2): 3-6.

Hossain, M. S., Urbi, Z., Sule, A., Rahman, K. M. H. (2014). Review article: *Andrographis paniculata* (Burm. f.) Wall. ex Nees: A Review of Ethnobotany, Phytochemistry, and

Pharmacology. The Scientific World Journal, 2014: 1 – 28.

Humbal, A., Chaudhary, N., Vaise, S., Pathak, B. (2021). A brief review on phytochemical and pharmacological aspects of *Andrographis paniculata*. Lupine Online Journal of Pharmacology and Clinical Research, 2(5): 264-269.

Imo, C., Arowora, K.A., Ezeonu, C.S., Ikwebe, J., Yakubu, O.E. et al. (2021). Biochemical and histological effects of ethanolic extracts of fruits of Xylopia aethiopica and seeds and leaves of Piper guineense on liver and kidney function in male albino rats. Future Journal of Pharmaceutical Sciences, **7:**1-12.

Imo, C., Arowora, K.A., Ezeonu, C.S., Yakubu, O.E., Nwokwu, C.D., Azubuike, N.C., Sallah, Y.G. (2019). Effects of ethanolic extracts of leaf, seed and fruit of Datura metel L. on kidney function of male albino rats. Journal of Traditional and Complementary Medicine, 9(4): 271-277.

Isah, R.T., Mohammed, M.O., Muhammad, A.T., Sahabi, S.M., Umar, Z.U. et al. (2018). Effects of aqueous leaf extracts of Senna occidentalis on rat kidney. African Journal of Biomedical Research, 21(2): 225-230.

Jacques, D.T., Marc, K.T., Jedirfort, H.M., Pascal, K.S. (2016). Histological and biochemical evaluations of the liver and kidney of Wistar rats fed with fish meal of Sarotherodon melanotheron captured with Tephrosia vogelii's powder. African journal of biotechnology, 15(11): 417-422.

Karunamoorthi, K., Jegajeevanram, K., Vijayalakshmi, J., Mengistie, E. (2013). Traditional medicinal plants: a source of phytotherapeutic modality in resource-constrained health care settings. Journal of Evidence-Based Complementary and Alternative Medicine, 18(1): 67-74.

Khaleel, S.M., Almuhur, R.A., Al-Deeb, T.M., Jaran, A.S. (2021). Biochemical changes in the liver, kidney and serum of rats exposed to ethanolic leaf extract of Ziziphus spina-christi. Jordan Journal of Biological Sciences, 14(4): 45-58.

Mao, Q.Q., Xu, X.Y., Cao, S.Y., Gan, R.Y., Corke, H., Beta, T., Li, H.B. (2019). Bioactive compounds and bioactivities of ginger (Zingiber officinale Roscoe). Foods, 8(6): 185-199.

Mishra, R.K., Kumar, A., Kumar, A. (2012). Pharmacological activity of *Zingiber officinale.* International Journal of pharmaceutical and chemical sciences, 1(3): 1073-1078.

Moghadamtousi, S. Z., Fadeinasab, M., Nikzad, S., Mohan, G., Ali, H. M. *et al.* (2015). *Annona muricata* (Annonaceae): A Review of Its Traditional Uses, Isolated Acetogenins and Biological Activities. International Journal of Molecular Sciences, 16: 15625 – 15658.

Mutar, T.F., Tousson, E., Hafez, E., Abo Gazia, M., Salem, S.B. (2020). Ameliorative effects of vitamin B17 on the kidney against Ehrlich ascites carcinoma induced renal toxicity in mice. Environmental Toxicology, 35(4): 528-537.

Natania, K., Haniel, K. (2021). Bitterness reduction of Green Chiretta (Andrographis paniculata) leaves and its functionality. In *IOP Conference Series:* Materials Science and Engineering, 1011(1): 012-036.

Nyeem, M. A. B., Mannan, M. A., Nuruzzaman, M., Kamrujjaman, K. M., Das, S. K. (2017). Indigenous king of bitter (Andrographis paniculata): A review. Journal of Medicinal Plants Studies, 5(2): 318 – 324.

Onyeanusi, B.I., Adeniyi, A.A., Onyeanusi, C.G., Ayo, J.O., Ibe, C.S. (2009). A study of the kidney of the Wistar Rat in Northern Guinea Savannah zone: the morphometric aspect. Pakistan Journal of Nutrition, 8(7): 1040-1042.

Sivakumar, V., Rajeshkumar, S. (2015). Protective effect of Andrographis paniculata on hyperglycemic mediated oxidative damage in renal tissues of diabetic rats. Journal of Phytopharmacology, 4(6): 287-294.

Subramanian, R., Zaini Asmawi, M., Sadikun, A. (2012). A bitter plant with a sweet future? A comprehensive review of an oriental medicinal plant: *Andrographis paniculata*. Phytochemistry reviews, 11: 39-75.

Wakchaure, R., Ganguly, S. (2018). Phytochemistry and pharmacological properties of ginger (*Zingiber officinale*), In: Mahdi, A. A., Abod, M., Khan, A. A., Ansair, M. I. and Maheshwari, R. K. (ed) Molecular Biology and Pharmacognosy and Beneficial Plants, ISBN 978-93-85995-56-9.

Zubaidi, S.N., Mohd N.H., Ahmad K.M.S., Abdul Q.T., Maarof, S. et al. (2023). Annona muricata: Comprehensive Review on the Ethnomedicinal, Phytochemistry, and Pharmacological Aspects Focusing on Antidiabetic Properties. Life, 13(2): 353-369.