PROTECTIVE EFFECTS OF EXTRACTS FROM *Garcinia kola* AGAINST ALUMINUM-INDUCED HEPATORENAL TOXICITY IN ALBINO RATS

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Abstract: Several health challenges result from environmental pollution by aluminum containing compounds. The liver and kidney are targets for aluminum toxicity. *Garcinia kola* is used in traditional medicine for the treatment of many diseases including liver and kidney damage. The current study was designed to investigate the effects of *Garcinia kola* extracts on biomarkers of liver and kidney damage in a rat model for aluminum toxicity. Twenty five (25) male albino rats were allocated to five (5) groups of five (5) rats each. Group 1 served as normal control and received normal saline while group 2 served as negative control and received daily oral administration of 100 mg/kg bw $AlCl_3$. Group 3-5 received 100 mg/kg bw $AlCl_3$ and extracts of *Garcinia kola* as follows: 200 mg/kg bw petroleum ether extracts, 200 mg/kg bw methanol extracts, 200 mg/kg bw defatted residue respectively. All treatments were administered orally and daily for 42 days. $AlCl_3$ induced a significant ($p<0.05$) increase in the levels of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), urea and creatinine. Treatment with petroleum ether and methanol extracts of *Garcinia kola* countered the effect of aluminum evidenced by the significant decrease ($p<0.05$) in the activity of the biomarkers. Defatted residue of *Garcinia kola* had the least effect on the parameters tested. The results obtained from this study revealed that extracts of *Garcinia kola* could protect the liver and kidney from aluminum toxicity.

Keywords: *Garcinia kola*, aluminum, hepatorenal, hepato-protection

Introduction

Aluminum is one of the most abundant elements on earth. It is a common component of medications, cosmetics, cooking utensils and food additives (Han *et al.*, 2013). It is toxic when absorbed into the body and accumulates in vital organs such as the liver, kidney, brain and heart. Consequently, aluminum can disrupt homeostasis in the vital organs which may involve genotoxic effects (Okail *et al.*, 2020; Afolabi *et al.*, 2020). There are abundant evidences to show that aluminum can cause biochemical and physiological dysfunction by promoting the production of reactive oxygen species and alteration in the levels of vital enzymes and metabolites (Farombi and Owoeye, 2011).

Garcinia kola is a forest plant found in West and Central Africa (Ekene *et al.*, 2014). In Nigeria it is called Namijingoro in Hausa, Igoligo in Igala and Idoma, orogbo in Yoruba and in Igbo, it is called aki-ilu (Fapohunda *et al.*, 2017). Seeds of *Garcinia kola* are rich in alkaloids, saponins, tannins, flavonoids, glycosides, sterols and phenols. The major constituents of the plant its biflavanoid contents including kolaviron and kolaflavanone (Iwu, 1985; 1986). *Garcinia kola* seeds have been proven through experiments to possess several medicinal properties including but not limited anti-diabetic, anti-cancer, anti-ulcer, anti-bacterial, anti-fungal and anti-viral activities (Farombi and Owoeye, 2011). Other literature support potency of extracts from *Garcinia kola* against chemical toxicants (Oyagbemi *et al.*, 2017; Adedara *et al.*, 2015; Owoeye *et al.*, 2015).

In the present study, the protective effect of extracts from *Garcinia kola* against aluminum-induced hepatorenal toxicity in albino rats is investigated.

Materials and Methods

Reagents and chemicals

Aluminium chloride was manufactured by Sigma Aldrich Chemical Co., Saint Louis, MO USA. Diagnostic kits for alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alanine phosphatase (ALP), urea and creatinine were products of Randox Laboratories Ltd., United Kingdom.

Collection and identification of plant material

Fresh seeds of *Garcinia kola* were purchased from the market in Anyigba, Kogi State, Nigeria and were thereafter authenticated in the Department of Plant Science and Biotechnology, Kogi State University, Anyigba, Nigeria.

Preparation of seeds extracts

The seeds were dehusked, washed, chopped into smaller pieces and the seed was air-dried and pulverized to a fine powder using a mechanical blender. The powdered seeds were extracted with light petroleum ether (b.p. 40-60^{0}C) in a Soxhlet extractor for twenty-four hours (24 h). The defatted dried marc was repacked and then extracted using methanol according to the method of (Adaramoye *et al.*, 2015). The methanol extract was evaporated to dryness and stored at 4°C. The solid material left after extraction with petroleum ether and methanol is henceforth referred to as residue.

Animal management

A total of twenty five (25) mature male albino rats weighing 165 – 200 g were obtained from the animals breeding and care facility of Federal University of Agriculture Makurdi, Benue State, Nigeria. The animals were kept in standard rat cages at room temperature (25 ± 4^{o}C) with a normal 12 h light/dark cycle and received standard commercial pelleted rat chow and water *ad libitum*. The rats were housed in the animal house facility, department of Biochemistry Kogi State University Anyigba. The rats were allowed to acclimatize for a period of 14 days. Handling and treatments of rats was in conformity to the guidelines of the National Institute of Health (NIH publication 85-23, 1985) for laboratory animal care and use.

Animal grouping and treatments

Twenty five (25) male albino rats were allocated to five (5) groups of five (5) rats per group. All treatments were done orally daily for 42 days as follows:

Group 1- Normal control received normal saline
Group 2- Aluminum 100 mg/kg bw
Group 3- Aluminum 100 + 200 mg/kg bw petroleum ether extracts
Group 4- Aluminum 100 + 200 mg/kg bw methanol extracts
Group 5- Aluminum 100 + 200 mg/kg bw defatted residue

The time difference between administration of aluminum and *Garcinia kola* extracts was 12 h.

Biochemical analysis

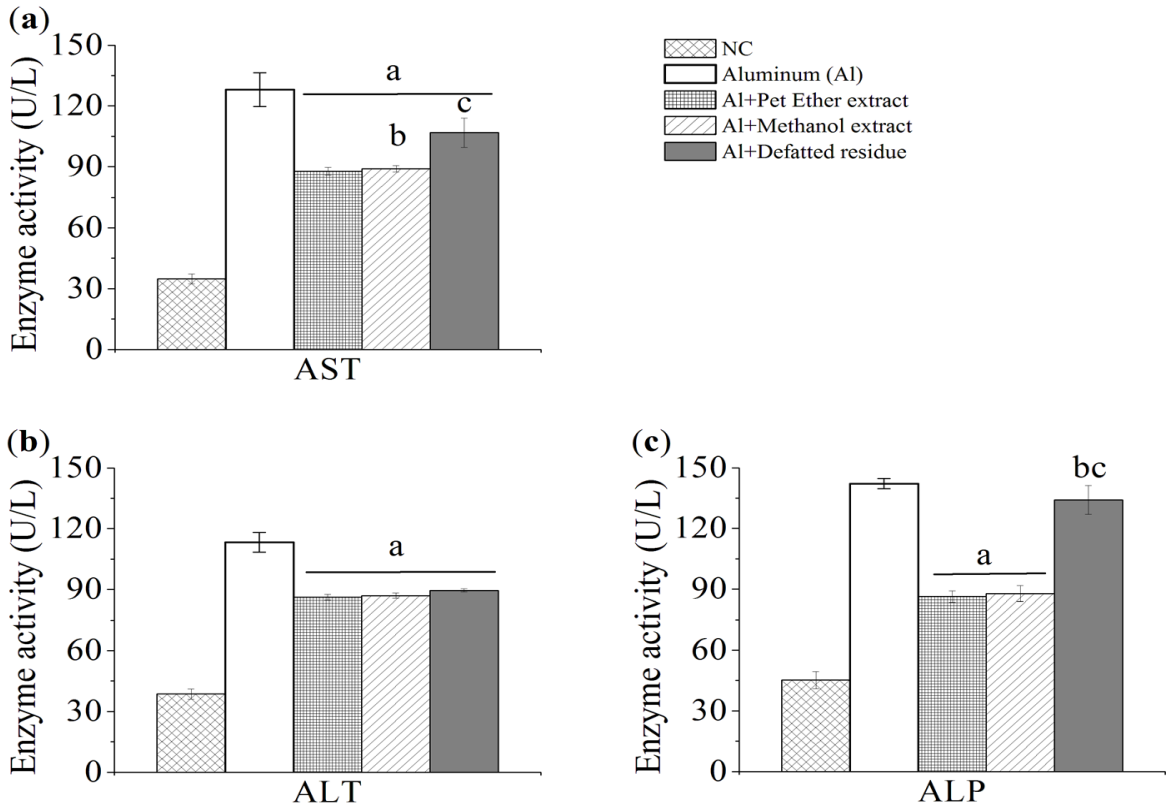
On the 43rd day of treatments the rats were sacrificed by cervical dislocation. Blood was collected by cardiac puncture, centrifuged at 3,000 g for 10 min to separate serum. Assessment of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), urea and creatinine was carried out based on manufactures instruction of Randox diagnostics kits.

Statistical analysis

Graph Pad Instat software was used for this analysis. The results are expressed as Mean ± SEM. The difference between groups was analyzed by one-way analysis of variance (ANOVA), the results were considered significant at $P < 0.05$.

Results and Discussion

The present study evaluated the protective effects of extracts from *Garcinia kola* on aluminum induced hepatorenal toxicity in albino rats. Oral administration of $AlCl_3$ resulted in a significant increase ($p<0.05$) in the activities of liver enzymes namely: ALT, AST and ALP compared to the control animals in Group 1 (Fig. 1a – c). This is an indication of hepatic damage caused by $AlCl_3$ and in agreement with previous research findings (Okail *et al.*, 2020; Afolabi *et al.*, 2020). Liver is the primary organ responsible for the detoxification of harmful xenobiotics. However, in the presence of high concentration of harmful compounds, the liver could surfer insult resulting in necrosis, fibrosis or complete loss of function (Balgoon, 2019). Damage to the hepatocytes involves disruption of membrane permeability and leakage of enzymes into the blood which explain the high levels of liver enzymes upon administration of $AlCl_3$ (Fig. 1a – c). Administration of *Garcinia kola* extracts significantly decreased ($p<0.05$) the activities of the liver enzymes. It is possible that the *Garcinia kola* has membrane stabilizing property that protects hepatocytes from been leaky (Salemcity *et al.*, 2016; Omole *et al.*, 2018). Hepatoprotection could also be due to the effect of phytochemicals from *Garcinia kola* mimicking the molecular signaling pathways of COX-2, Nrf-2 and NF-kB (Farombi *et al.*, 2009; Ahmed *et al.*, 2017). The potency of petroleum ether and methanol extracts was similar and higher than that of the defatted extract. The lower potency of the defatted extract may be due to the loss of important medicinal compounds in the process of defatting and methanol solvent extraction.



*NC: normal control; AST: aspartate transaminase, ALT: alanine transaminase, ALP: alkaline phosphatase; Values are expressed a mean of five replicates± SEM; a<0.05 compared with Aluminum group; b<0.05 compared with Al + 200 mg/kg Petroleum ether extract group; c<0.05 compared with Al + 200 mg/kg Methanol extract group

Fig. 1: Variations in activity of liver enzymes AST- aspartate amino transferase (a), ALT-alanine amino transferase (b), and ALP- alkaline phosphatase (c) of aluminum poisoned rats treated with extracts of *Garcinia kola*

Urea and creatinine are two nitrogenous compounds used to assess the functions of the kidney. The kidney is a target for aluminum accumulation and toxicity. High levels of urea and creatinine in the blood is indicative of impaired renal function. The results of the kidney function of aluminum poisoned rats treated with extracts of *Garcinia kola* are shown in Table 1. The present study showed that administration of $AlCl_3$ resulted in significant increase of urea and creatinine levels. The biochemical change is in consonance with the results of Galal *et al.*, (2019).

Table 1: Kidney function markers of aluminum poisoned rats treated with extracts of *Garcinia kola*

Groups	Biomarker	
	Urea mg/dl	Creatinine mg/dl
Normal control	22.80 ± 1.49^{a}	0.20 ± 0.02^{a}
Aluminium 100 mg/kg bw	52.20 ± 0.86^{b}	0.90 ± 0.04^{b}
Al + Pet Ether Extract 200 mg/kg bw	38.60 ± 2.21^{c}	0.60 ± 0.04^{c}
Al + MeOH Extract 200 mg/kg bw	39.40 ± 1.29^{c}	0.70 ± 0.04^{d}
Al + Residue 200 mg/kg bw	49.60 ± 0.81^{b}	0.70 ± 1.67^{d}

Values are expressed a Mean of five replicates ± SEM; Values with the different superscript on the same column are significantly different at $p<0.05$

In this study, the protective effect of extracts of *Garcinia kola* was observed as it significantly decreased ($p<0.05$) serum levels of urea and creatinine compared to the group that received aluminum alone. This may be due to improved glomerular filtration (Galal *et al.,* 2019; Okail *et al.,* 2020). This is in accordance with the findings of Adaramoye *et al.* (2016) and Alabi *et al.* (2018) which demonstrated the nephroprotective effective of *Garcinia kola* against anti-tubercular drugs and diclofenac toxicity, respectively. Again, the defatted residue offered the least protection probably due to the aforementioned reason.

Conclusion

It could therefore be concluded that *Garcinia kola* extracts may offer protection against hepatorenal dysfunction. However, further studies will be required to evaluate molecular mechanisms involved in the protection of hepatic and renal health by *Garcinia kola* extracts.

Abbreviations

AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase; COX-2: cyclooxygenase-2; Nrf-2: Nuclear factor erythroid 2- related factor 2; NF-kB: Nuclear factor kappa B

Conflict of Interests

The authors declare that they have no competing interests.

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References

Adaramoye OA, Kehinde AO, Adefisan A, Adeyemi O, Oyinlola I &Akanni OO 2016. Ameliorative effects of kolaviron, a biflavonoid fraction from garcinia kola seed on hepato-renal toxicity of anti-tuberculosis drugs in wistar rats. *Tokai J. Exp. Clin. Med.*, 41(1): 14-21.

Adedara IA, Owoeye O, Aiyegbusi MA, Dagunduro JO, Daramola YM & Farombi EO 2015. Kolaviron protects against benzo[a]pyrene-induced functional alterations along the brain-pituitary-gonadal axis in male rats. *Envt. Toxicol. Pharmacol*., 40(2): 459-470.

Afolabi AA, Ashamu EA & Oluranti OI 2020. Ameliorative effect of *Psidiumguajava* leaf aqueous extract on aluminium nitrate-induced liver damage in female Wistar rats. *Clin. Phytosci.*, 6: 51.

Ahmed SMU, Luo L, Namani A, Wang XJ & Tang X 2017. Nrf2 signaling pathway: Pivotal roles in inflammation. *Biochimicaet Biophysica Acta*, 1863(2): 585-597.

Alabi QK, Akomolafe RO, Adefisayo MA, Olukiran OS, Nafiu AO, Fasanya MK & Oladele AA 2018. Kolaviron attenuates diclofenac-induced nephrotoxicity in male Wistar rats. *Appl. Physiol. Nutr. Metab.*, 43(9): 956-968.

Balgoon MJ 2019. Assessment of the protective effect of *Lepidiumsativum* against aluminum-induced liver and kidney effects in albino rat. *Bio. Med. Res. Int.*, Article ID 4516730, doi.org/10.1155/2019/4516730.

Ekene EN & Erhirhie EO 2014. Department of pharmacology and therapeutics, Faculty of Basic Medical Sciences, Delta State University, Abraka, Delta State, Nigeria. Garcinia kola: A review of its ethnomedicinal, chemical and pharmacological properties. *Int. J. Current Res. and Rev.*, 06: 11.

Fapohunda S, Arinola A, Otuneme O, Adaramola B, Jegede D, Adewumi A, Alosheinloye A & Adebayo O 2017. Evaluation of the nutraceutical potential of Garcinia kola seed oil.*Journal of Pharmacognosy and Phytochemistry*, 6(5):1894-1901.

Farombi EO, Shrotriya S & Surh YJ 2009. Kolaviron inhibits dimethyl nitrosamine-induced liver injury by suppressing COX-2 and iNOS expression via NF-kappaB and AP-1. *Life Sci.*, 84(5-6): 149-55.

Farombi EO & Owoeye O 2011. Antioxidative and chemopreventive properties of *Vernonia amygdalina* and *Garcinia biflavonoid*. *Int. J. Envt. Res. Public Health*, 8(6): 2533-55.

Galal SM, Hasan HF, Abdel-Rafei MK & El Kiki SM 2019. Synergistic effect of cranberry extract and losartan against aluminium chloride-induced hepatorenal damage associated cardiomyopathy in rats. *Arch. Physiol. Biochem*., 125(4): 357-366.

Han S, Lemire J, Appanna VP, Auger C, Castonguay Z & Appanna VD 2013. How aluminum, an intracellular ROS generator promotes hepatic and neurological diseases: the metabolic tale. *Cell Biology and Toxicology*, 29: 75-84.

Iwu MM 1985. Antihepatoxic constituents of *Garcinia kola* seeds. *Experientia*, 41(5): 699-700.

Iwu MM 1986. Biflavanones of Garcinia: Pharmacological and biological activities. *Prog. Clin. Biol. Res*., 213: 485-488.

Okail HA, Ibrahim AS & Badr AH 2020. The protective effect of propolis against aluminum chloride-induced hepatorenal toxicity in albino rats. *JoBAZ.*, 81: 34.

Omole JG, Ayoka OA, Alabi QK, Adefisayo MA, Asafa MA, Olubunmi BO & Fadeyi BA 2018. Protective effect of kolaviron on cyclophosphamide-induced cardiac toxicity in rats. *J. Evidence-based Integrative Med.*, 23: 1-11.

Owoeye O, Adedara IA, Adeyemo OA, Bakare OS, Egun C & Farombi EO 2015. Modulatory role of kolaviron in phenytoin-induced hepatic and testicular dysfunctions in Wistar rats. *J. Diet Suppl.*, 12(1): 105-117.

Oyagbemi AA, Omobowale TO, Olopade JO & Farombi EO 2017. Kolaviron and *Garcinia kola* attenuate doxorubicin-induced cardiotoxicity in Wistar rats. *J. Complement Integr. Med*., 15(1): doi:10.1515/jcim-2016-0168.

Salemcity AJ, Attah AT, Oladimeji O, Olajuyin AM, Usifo G &Audu T 2016. Comparative study of membrane-stabilizing activities of kolaviron Dryopterisfilix-mas and *Ocimumgratissimum* extracts. *Egypt Pharmac. J.*, 15: 6-9.