



Ameliorating Effect of Methanol Extract of Finger Root Bark (*Uvaria chamae*) on some Selected Biochemical Parameters of CdCl₂ Induced Toxicity in Wistar Rats

**George C. Njoku^{a*}, Prisca C. Aririguzo^b, Emmanuel K. Amanze^c,
Isabel C. Nwagu^a, Chizurum P. Christian^d and Agbagwara C. Queendarlyn^e**

^a Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

^b Department of Public Health, School of Health Technology, Federal University of Technology Owerri, PMB 1526, Owerri, Imo State, Nigeria.

^c Department of Microbiology, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, PMB 7267, Umuahia, Abia State, Nigeria.

^d Department of Microbiology, Faculty of Biological Science, Abia State University, Uturu, Abia State, Nigeria.

^e Department of Biochemistry, Faculty of Biological Science, Imo State University, Samek Rd, 460108, Owerri, Imo State, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author GCN conceived the presented idea, developed the theory, performed the computations, contributed to interpreting the results and wrote the manuscript. Author PCA experimented and also wrote the manuscript. Author EKA experimented and also wrote the manuscript. Author ICN contributed to the design and implementation of the research, the analysis of the results and the manuscript's writing. Author CPC performed the analytic calculations and performed the numerical simulations. Author ACQ experimented and carried out the practical. All authors provided critical feedback and helped shape the research, analysis and manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JOCAMR/2022/v18i130342

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/86667>

Original Research Article

**Received 25 February 2022
Accepted 05 May 2022
Published 09 May 2022**

ABSTRACT

Background: High cadmium-induced injuries have necessitated the search for potent and cost-effective herbal management models. Hence, this study aimed at evaluating the ameliorating effect of methanol extract of finger root bark (*Uvaria chamae*) on some selected biochemical parameters of cadmium-induced toxicity in Wistar rats.

Methods: Thirty (30) Male rats weighing 84- 183 grams were obtained and kept in the animal house to acclimatize for eight (8) days prior to the experiment. The rats were grouped into five groups containing six rats each. Group 1 served as normal control; group 2 served as the negative control treated with 10mg/kg bw CdCl₂; group 3 contained rats fed with 500mg/kg bw plant extract; Group 4-5 contained cadmium-intoxicated rats treated with *Uvaria chamae* (250mg/kg body weight and 250mg/kg body weight) respectively for 13 days. Thereafter, the rats were sacrificed, and blood samples were collected through the ocular puncture for biochemical analysis. Activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), as well as lipid profiles were assessed. Tissue antioxidant levels of reduced glutathione (GSH), malondialdehyde (MDA), and activities of antioxidant enzymes such as superoxide dismutase (SOD) were also determined.

Result: CdCl₂ caused a significant derangement in lipid profile, increasing serum triglyceride, total cholesterol and low-density lipoprotein (LDL) while high-density lipoprotein (HDL) level was diminished. Liver biomarkers (ALT, AST, ALP) were also significantly elevated in the serum relative to the control animals following exposure to CdCl₂. Activities of antioxidant enzymes in the serum were markedly inhibited by CdCl₂ exposure. Treatment with *Uvaria chamae* extract caused a dose-dependent restoration of all biochemical parameters determined.

Conclusion: The findings show the potential usefulness of *Uvaria chamae* extract in managing certain diseases.

Keywords: Biomarkers; cadmium; oxidative stress; lipid; liver.

ABBREVIATIONS

ALP : Alkaline phosphate
 ALT : Alanine Amino Transferase
 AST : Aspartate Amino Transferase
 CdCl₂ : Cadmium Chloride
 GSH : Glutathione
 H₂O₂ : Hydrogen peroxide
 HDL-Ch: High-Density Lipoprotein Cholesterol
 LDL-Ch: Low-Density Lipoprotein Cholesterol
 MDA : Malondialdehyde
 OECD : Organization for Economic Cooperation and Development
 ROS : Reactive oxygen species
 SOD : Superoxide Dismutase

1. INTRODUCTION

Environmental pollution has remained an indispensable makeup of our general surroundings today. According to Guo et al. [1], it is an unpleasing modification of our environment entirely due to man's direct and indirect activities on organisms' energy patterns, radiation levels, and chemical and physical components. Since the late 19th and early 20th centuries, metals have had a tremendous rise in environmental pollution. The environmental constituents, including the biosphere, have been constantly

threatened by extravagant contamination of heavy metals emitted from various industries. Many of these heavy metals have been reported to have adverse effects [2]. Cadmium (Cd) is a toxic, naturally occurring, non-essential transition metal. Cadmium appears as a pollutant derived from various commercial sources in the environment. Due to its high toxicity, it has remained a risk to the health of both plants and human beings. According to Hideaki et al. [3], studies have shown that excessive cadmium exposure interferes with DNA repair, induces genomic stability, and improves the generation of reactive oxygen species. The presence of cadmium in cells disrupts cellular activities, including cell differentiation, proliferation, and apoptosis. The most dangerous characteristic of cadmium is that it accumulates throughout a lifetime due to its long biological half-life. In animal models, some plants have proven to reduce plasma levels of TC, TG and LDL-C [4]. Various researchers have proposed medicinal plants to be an alternative remedy to eliminate the biochemical implications caused by cadmium toxicity.

Finger Root (also known as *Uvaria chamae*) is a yellow fruit comprised of a non-poisonous pulp and known to be widely consumed. In

Nigeria, *Uvaria chamae* is locally called Kaskaifi or Lukuki by the Hausa, MmimiOhea by the Igbos and Oko-oja by the Yoruba in Nigeria [5]. The roots of *Uvaria chamae* have been reported to treat various health issues, including inflammation of the Mucous membrane, bronchitis and gonorrhoea, dysentery, fever, and relieve childbirth pains [6]. etc. *Uvaria chamae* has been reported to have antibacterial, cytotoxicity [7], antimalarial, hepatoprotective and antiviral properties [7]. Using *Uvaria chamae* to remedy cadmium intoxicated Wistar rats has never been accounted for. Hence, this study investigates *Uvaria chamae* ameliorating potentials in some selected biochemical parameters in CdCl₂ induced toxicity in Wistar rats.

2. MATERIALS AND METHODS

2.1 Collection of Plant Samples

Finger roots (*Uvaria chamae*) were collected from the premises of the Umuebele community in Oyibo Local Government Area of Rivers State. The plant was identified by a botanist from the forestry department, Federal University of Technology Owerri PMB 1526, Owerri, Imo State, Nigeria, and the voucher specimen was deposited in the department's herbarium with the voucher specimen Voucher No. IHF=22126.

2.2 Preparation of Plant Sample Extract

The preparation of the plant extract adopted the method described by Madubunyi [8]. The Finger roots (*Uvaria chamae*) were washed thoroughly and air-dried at room temperature (20±27°C). They were pulverized using a hand milling machine (TSK-948 West Point, France). The methanol extract of *Uvaria chamae* was prepared using 500g of the powdered leaves mixed in 1839ml of methanol for 70 hours with occasional stirring. The mixture was filtered using a muslin cloth and then with Whatman filter

paper No.1. The chaff was discarded, and the filtrate was evaporated and dried using a rotary evaporator (Cole-Parmer model SB-1200) at 60°C. The filtrate was stored in the refrigerator until it was ready for use.

2.3 Experimental Animal

Thirty (30) male Wistar rats (84-183g) were purchased from an animal farm at the University of Nigeria Nsukka and used for this study. The rats were housed in standard aluminium cages (6 animals per cage) in clean conditions at an ambient temperature of 25°C with a 12-hour light /dark cycle. The rats were fed with water *ad libitum* and a commercialized poultry feed called "Chikun feed". The rats were acclimatized for 8 days before the commencement of the experiment. The Principles of Laboratory Animal Care, NIH [9], were followed throughout this study. All experimental procedures were conducted according to the animal ethics committee.

2.4 Preparation of Cadmium Chloride Solution and *Uvaria chamae* Root Extract

The method described by Al-Hashem et al. [10] was employed. Cadmium chloride (CdCl₂) was dissolved in sterile distilled water to ascertain a required concentration of which the rats received an equivalent of 1.0ml, which was administered orally with a cannula. *Uvaria chamae* extract was reconstituted in distilled water to achieve the desired doses of 250 and 500 mg/kg body weight used in the animal experiment.

2.5 Experimental Design

The rats were allowed to acclimatize for 8 days before the commencement of treatment. The animals were marked and divided into five groups (1-5) of six (6) rats per group.

Table 1. Grouping and Treatment of Animals

Groups	Treatment	Duration
Group 1	Feed + H ₂ O at 5ml/kg	13 days
Group 2	10mg/kg body weight of cadmium chloride (CdCl ₂)	13 days
Group 3	500mg/kg body weight of <i>Uvaria chamae</i> extract	13 days
Group 4	10mg/kg body weight of CdCl ₂ + 250mg/kg body weight of <i>Uvaria chamae</i> extract	13 days
Group 5	10mg/kg body weight of CdCl ₂ + 500mg/kg body weight of <i>Uvaria chamae</i> extract	13 days

2.6 Acute Oral Toxicity

The acute oral toxicity of the plant extract was carried out strictly in adherence to the Organization for Economic Cooperation and Development (OECD) guidelines. Four male rats per dose were used for the experiment. Overnight fasted rats were orally fed with the methanol extract of *Uvaria chamae* in dose levels of 200, 800, and 1000 mg/kg body weight, respectively. The rats were consciously observed for their behavioural, touch response, pain response and spontaneous activity, and autonomic (defecation and urination) profiles for 24 h. After 24 h, the rats were observed for 14 days for mortality.

2.7 Collection and Preparation of Samples

At the end of the administration period, the animals were anaesthetized on the 14th day, and blood samples were collected via ocular puncture. The blood samples were stored in clean vacutainer tubes and centrifuged at 4000 g for 15 minutes. The serum was used to estimate biochemical markers using Randox Diagnostic kits.

2.8 Determination of Biochemical Parameters

The plasma samples were used for the determination of alanine transaminase (ALT), aspartate transaminase (AST) [11], as the liver function indicator, Malondialdehyde (MDA) [12], as the lipid peroxidation indicator, Superoxide Dismutase (SOD) [13], and Glutathione (GSH) as

the antioxidant enzymes. The Total plasma Cholesterol (T-Ch) [14], Triglycerides (TG) [15], High-Density Lipoprotein Cholesterol (HDL-Ch) [16].

2.9 Statistical Analysis

Data obtained was expressed as mean \pm SD and statistically analyzed using one-way analysis of variance (ANOVA) with Turkey's multiple comparison post hoc tests to compare the level of significance between the test groups. The values of $p < 0.05$ were considered significant.

3. RESULTS

3.1 Toxicity Study of *Uvaria chamae* extract

Acute toxicity studies showed no mortality up to 1000 mg/kg given as a single oral administration mg/kg. The study was done at three different dose levels (250 and 500 mg/kg).

3.2 Result of Methanol Extract of *Uvaria chamae* Root bark on Biochemical Parameter: alanine aminotransferase (ALT)

Data for the ALT enzyme activities were significantly ($p < 0.05$) increased in the untreated cadmium-intoxicated group (24.47 ± 0.66) compared to the normal control (20.08 ± 0.45). At 500mg/kg of the cadmium-intoxicated group treated group, the plant extract significantly decreased ALT compared to the normal control.

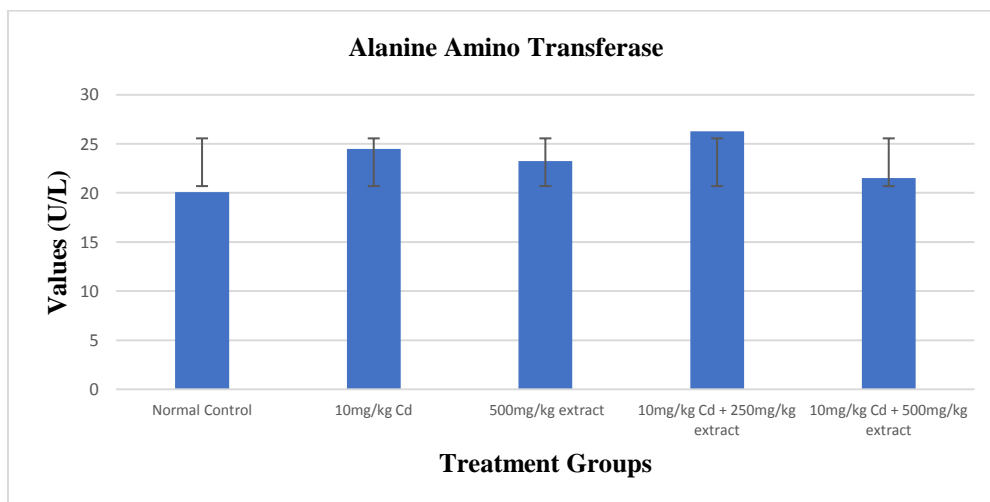


Fig. 1. Effect of *Uvaria chamae* Extract on Alanine Amino Transferase (ALT) serum enzymes
 Values are expressed as mean \pm SD (n=6). * $p < 0.05$ when compared with the normal control

3.3 Result of Methanol Extract of *Uvaria chamae* Root Bark on Biochemical Parameter: Aspartate Amino Transferase

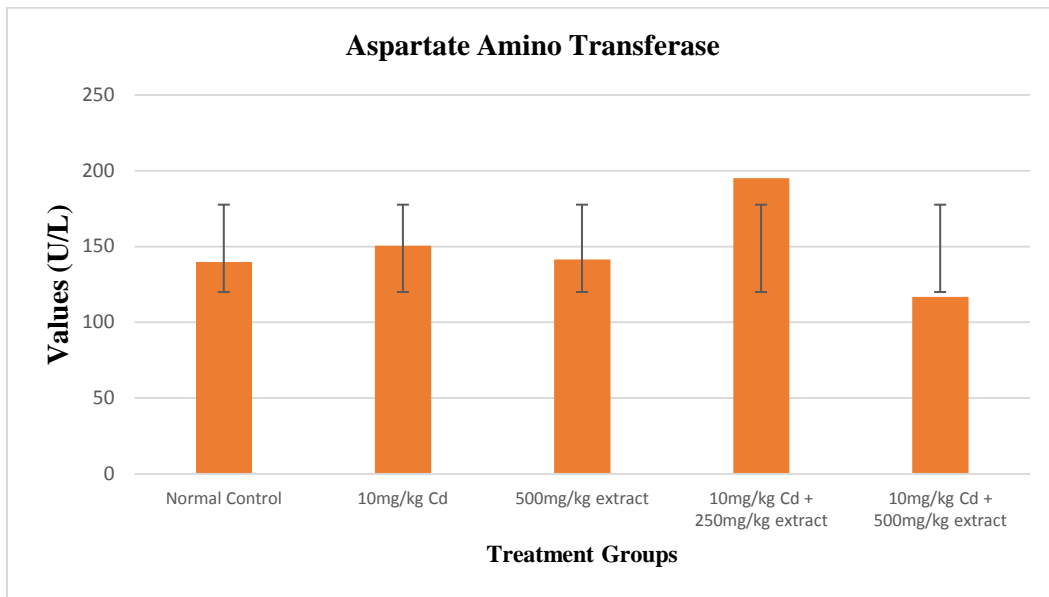


Fig. 2. Effect of *Uvaria chamae* Extract on Aspartate Amino Transferase (AST) serum enzymes
 Values are expressed as mean±SD (n=6). * $p < 0.05$ when compared with the normal control

The aspartate amino transferase (AST) activity of rats administered 10 mg/kg Cd + 250 mg/kg extract showed a significantly ($P < 0.05$) elevation compared to the normal control. There was no significant difference in the other groups extract 500mg/kg, cadmium 10mg/kg and Cadmium, 10 mg/kg + Extract, 500 mg/kg when compared to the control group.

3.4 Result of Methanol extract of *Uvaria chamae* Root bark on Biochemical Parameter: Alkaline phosphate

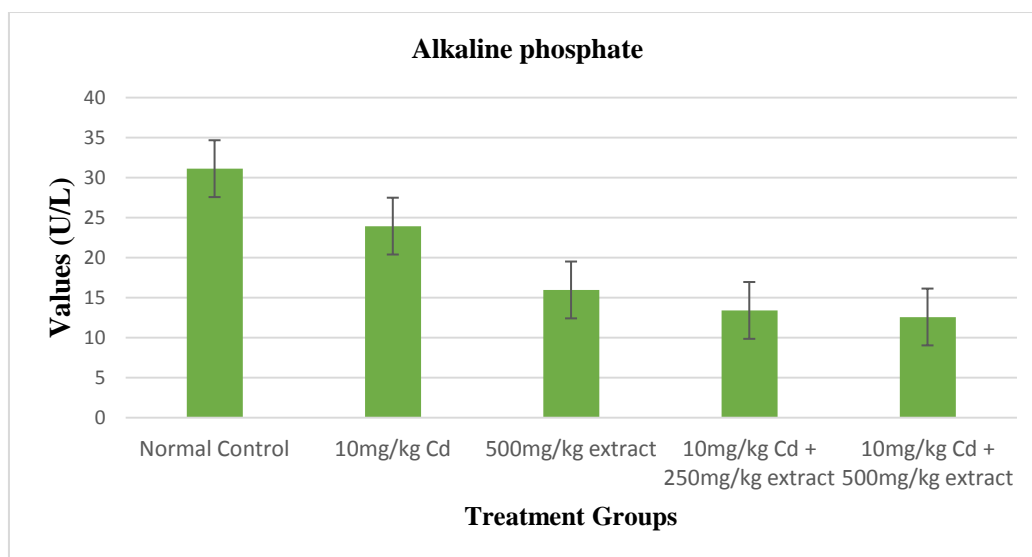


Fig. 3. Effect of *Uvaria chamae* Extract on Alkaline phosphate (ALP) serum enzymes
 Values are expressed as mean±SD (n=6). * $p < 0.05$ when compared with the normal control
 The alkaline phosphate (ALP) activity of rats administered from (Group 2-5) was significantly ($P > 0.05$) lower compared to the normal control

3.5 Result of the Methanol Extract of *Uvaria chamae* Root Bark on Biochemical Parameter: Malondialdehyde Concentration

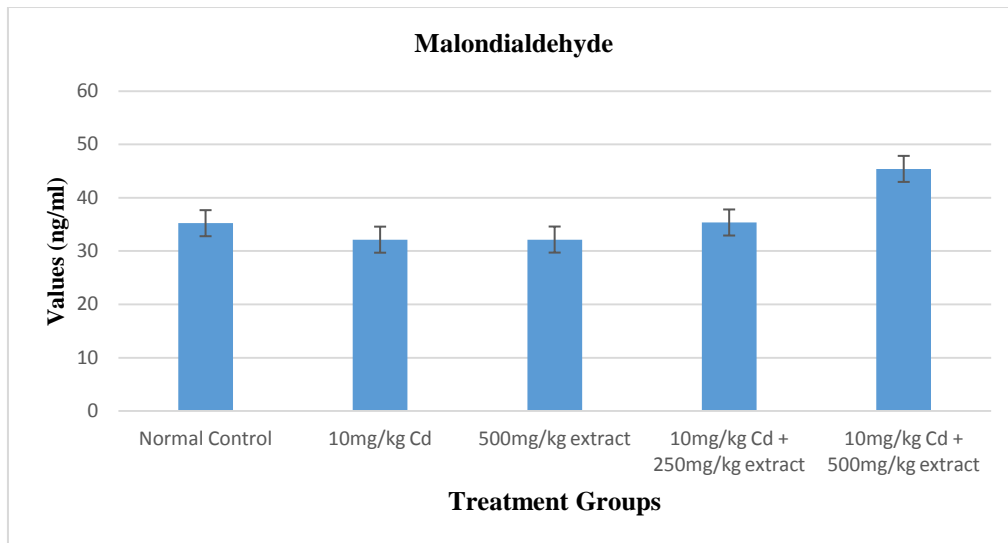


Fig. 4. Effect of *Uvaria chamae* extract on malondialdehyde (MDA) concentration of cadmium-intoxicated rats

Values are expressed as mean±SD (n=6). *p<0.05 when compared with the normal control

Data for the MDA enzyme activities were significantly ($p<0.05$) reduced in the cadmium-intoxicated group compared to the normal control. Supplementation of methanol extract of *Uvaria chamae* at 250 mg/kg and 500 mg/kg significantly elevated MDA activity compared to the control animals.

3.6 Result of the Methanol Extract of *Uvaria chamae* Root Bark on Biochemical Parameter: Superoxide Dismutase activity

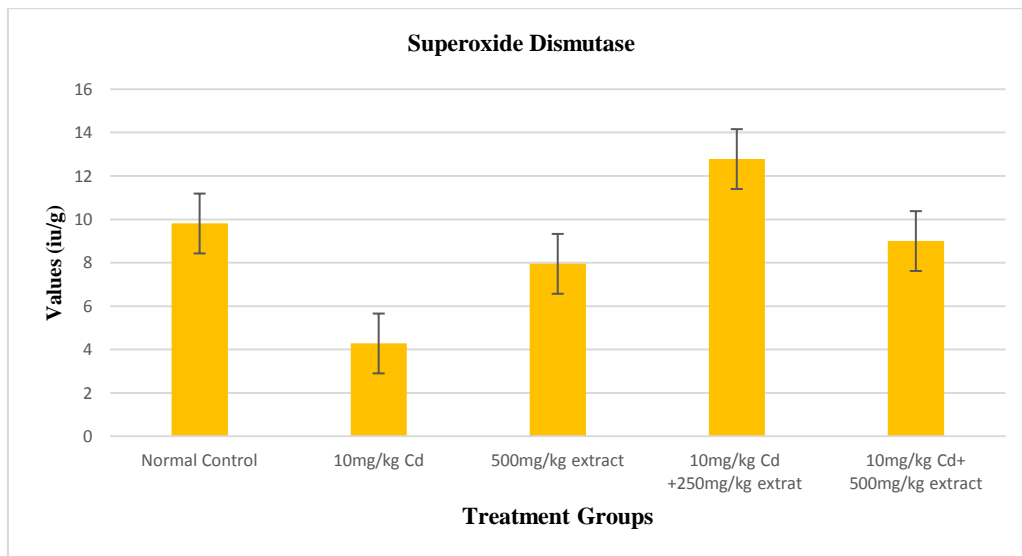


Fig. 5. Effect of *Uvaria chamae* Extract on Superoxide Dismutase (SOD) concentration of cadmium-intoxicated rats

Values are expressed as mean±SD (n=6). *p<0.05 when compared with the normal control

Data for the SOD enzyme activities were significantly ($p<0.05$) reduced in the cadmium-intoxicated group (4.28 ± 0.65) compared to the normal control (9.81 ± 1.10). However, supplementation of methanol extract of *Uvaria chamae* at 250 mg/kg and 500 mg/kg significantly elevated SOD activity compared to the control animals

3.7 Result of the Methanol extract of *Uvaria chamae* Root Bark on Biochemical Parameter: Glutathione Concentration

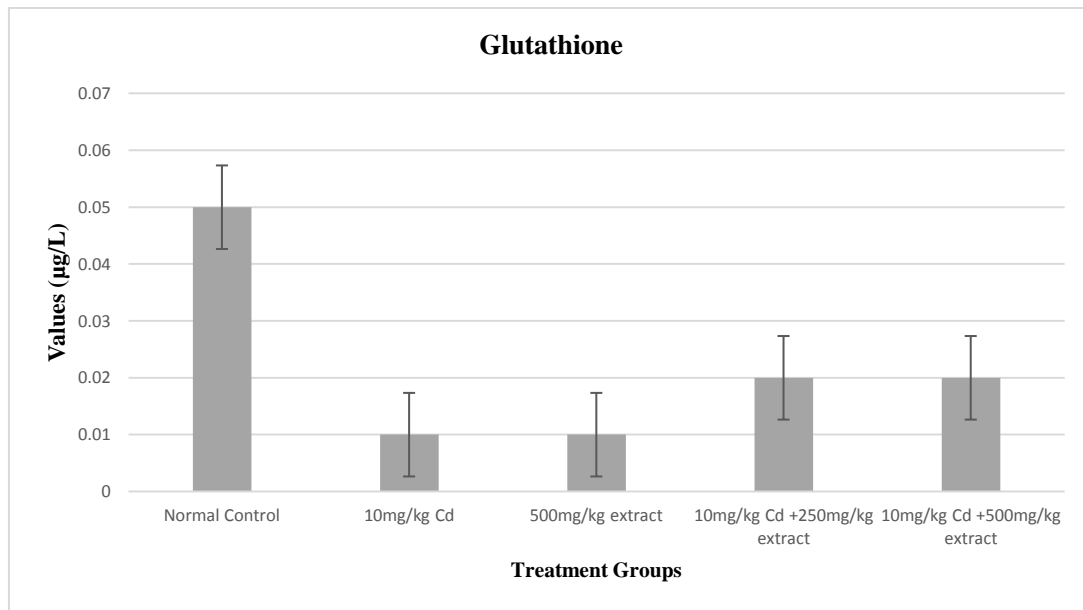


Fig. 6. Effect of *Uvaria chamae* Extract on Glutathione (GSH) Concentration of cadmium-intoxicated rats

Values are expressed as mean±SD (n=6). *p<0.05 when compared with the normal control
Data for the GSH enzyme activities were significantly (p<0.05) reduced in the cadmium-intoxicated group compared to the normal control. Supplementation of methanol extract of *Uvaria chamae* at 250 mg/kg and 500 mg/kg significantly elevated GSH activity compared to the control animals

3.8 Result of the Methanol Extract of *Uvaria chamae* Root Plant on the Lipid Profile Parameter of Cadmium-intoxicated Wistar Albino Rat

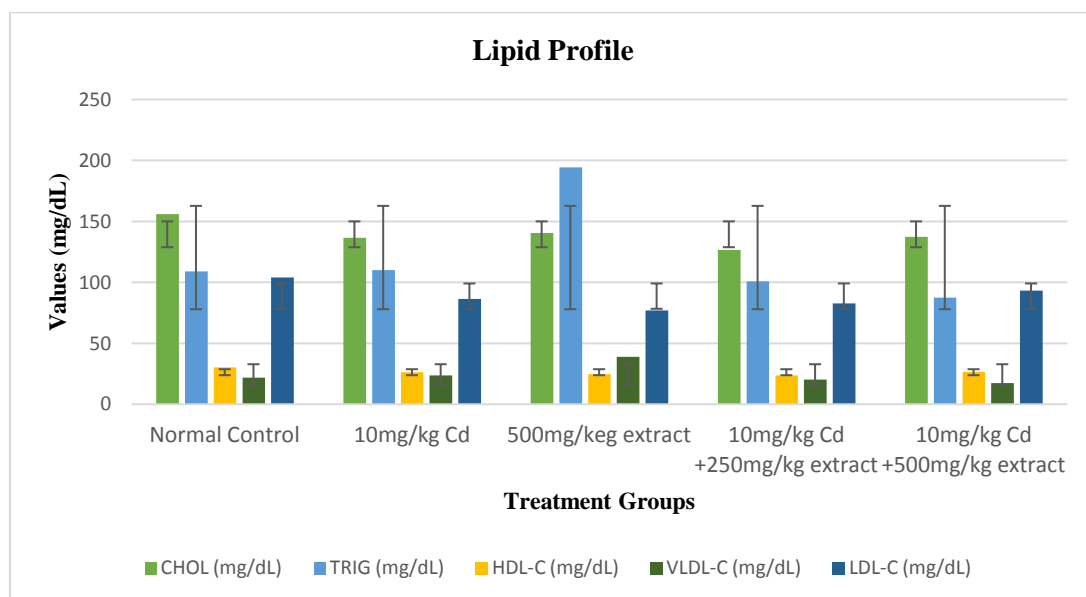


Fig. 7. Effect of *Uvaria chamae* extract on the lipid profile parameter of cadmium-intoxicated wistar albino rat

Values are expressed as mean ± SD (n=6). *p<0.05 when compared with the normal control

Exposure to CdCl₂ resulted in marked ($p < 0.05$) derangement in lipid profile in all tissues of experimental animals analyzed. Supplementation with *Uvaria chamae* extract caused a dose-dependent restoration of deranged lipid profile comparable to the normal control group.

4. DISCUSSION

This study evaluated the ameliorating effect of methanol extract of finger root bark (*Uvaria chamae*) on selected biochemical parameters of CdCl₂ induced toxicity in Wistar rats.

From our study, the exposure of experimental rats to CdCl₂ toxicity resulted in a significant elevation in the serum level of these biomarkers compared to the normal control. The rise in the serum levels of these biomarkers indicates free-radical induced oxidative damage to the hepatocytes, as shown by the serum levels of these biomarkers. A rise in the ALT level usually accompanies a rise in AST activity. ALP is an abundant enzyme in hepatocyte membranes and is used to screen for cholestasis or biliary obstructions [17]. The rise of these serum biomarkers during liver diseases is due to their occupancy in the hepatocyte. If the liver cells are damaged, they only leak into the bloodstream, and the spill-over of the enzyme into the blood is a good indicator of abnormal cell damage and a sign of severe liver disease [18]. ALT, AST and ALP were on the increase due to the exposure to cadmium-induced oxidative attack on the liver cells. However, treatment with *Uvaria chamae* extract showed significant dose-dependent (250mg/kg and 500 mg/kg plant extract) restoration of these biomarkers (ALT, AST and ALP) activities in the serum and tissue homogenates to the negative control. The result of the work was in agreement with the previous work of Madubunyi [8] and suggested the hepatoprotective potentials of *Uvaria chamae* extract, which can be utilized in the management of liver diseases.

Lipid peroxidation is an established mechanism of cellular injury and indicates oxidative stress in cells and tissues [19]. It is known that the quantity of MDA is an intensity index of the peroxidation process of poly-unsaturated fatty acids (PUFAs) contained in food [20]. There was a significant dose-dependent (250mg/kg and 500 mg/kg plant extract) increase in MDA concentration in the treated group relevant to the untreated group. These results suggest that the ethanol extract of *Uvaria chamae* can reverse

lipid peroxidation. The outcome of this work tallied with the previous findings made by Miaffo et al. [21], who reported a decrease in MDA level in rats administered with aqueous extract of the plant species *Combretum molle* twigs.

The primary defense against the superoxide anion is Superoxide dismutase (SOD), which converts the superoxide anion into hydrogen peroxide and water. Some studies suggest that over expression of SOD is harmful to cells [22]. Reactive oxygen species (ROS) present in many cells with overexpressed SOD have been attributed to elevated levels of hydrogen peroxide (H₂O₂) and accompanying oxidative damage resulting from hydroxyl radical formation [23]. In the present study, administration of CdCl₂-exposed animals with *Uvaria chamae* extract reactivated the activity of SOD in the serum, and this is in agreement with Nwobodo et al. [24].

Glutathione is a tri-peptide comprised of the amino acid L-cysteine, L-glutamic and glycine. Glutathione functions as a water-soluble antioxidant at the cellular level and is directly involved in specific detoxification reactions that protect the body against dangerous substances. Several shreds of evidence are present that Cd²⁺ is associated with oxidative stress because this metal can alter the antioxidant defense system in various tissues of animals, causing a depletion in the level of GSH and alteration in the activity of antioxidant enzymes and a change in the structure of cell membrane through a process of lipid peroxidation, this was stated by Cuypers et al. [25]. Cadmium may directly induce oxidative stress causing lipid peroxidation, resulting in protein modification and membrane gradient alteration, resulting in loss of integrity and irreversible damage [26]. A significant reduction in the level of GSH in the liver cells increases the hepatotoxicity caused by cadmium, which is in line with the research finding of Satarug et al. [27].

The result of this study revealed a significant ($p > 0.05$) decrease in the level of the enzyme parameter (GSH). Treatment with *Uvaria chamae* extract to the CdCl₂-exposed animals resulted in a significant dose-dependent elevation (250mg/kg and 500 mg/kg plant extract) compared to the normal control. The increase in the level of GSH in the treatment group indicates that the plant extract helped boost the GSH concentration in the cytosol, inducing oxidative stress. This result is in line with previous findings made by Asagba et al. [28], who reported that *Hibiscus sabdariffa*

anthocyanins are potent antioxidants and consonant with the reported protective effect of antioxidant nutrients against Cadmium-induced oxidative stress and lipid peroxidation in the liver and kidney.

Information on the susceptibility of the heart to atherosclerosis and its associated coronary heart disease could be provided by the cholesterol profile. [29].The reduction in HDL-C at all doses investigated may not be clinically beneficial to the animals since the rate at which high plasma cholesterol is carried to the liver was also decreased. Furthermore, the enhanced level of cholesterol and LDL-C may suggest cardiovascular risk in the animals. This is supported in the present study by increasing the computed atherogenic index, a helpful indicator of cardiovascular diseases [30].

5. CONCLUSION

From the results obtained from our study, we can conclude that the best dose of *Uvaria chamae* extracts that yield the best result with good efficacy and less hepatotoxicity on biomarker enzymes is 500 mg/kg. It could be a potential source of natural antioxidants that could be used as a therapeutic agent to prevent or treat degenerative diseases associated with oxidative stress. However, it is recommended that further studies be carried out to ascertain the therapeutical potency of this plant when used by humans.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Guo FY, Bi W, Guo FL, et al. Interannual Climate Variability in Shandong and Its Relationship with ENSO. *Oceanologia et Limnologia Sinica*, 2017;48:466-474.
2. Singh KP, Bhattacharya S, Sharma P. Assessment of heavy metal contents of some Indian medicinal plants. *Am-Eu, J. Agri. Env. Sci*, 2014;14:1125–1129. DOI:10.5829/idosi.aejaes.2014.14.10.12447
3. Hideaki U, Ashaolu VO, Ukwenya AB, Okonoboh OK, Ghazal AAG, Jimoh. *International J. of Medical Sci.* 2008;3(6):219-222.
4. Touiss I, Khatib S, Bekkouch O, Amrani S, Harnafi H. "Phenolic extract from *Ocimum Basilicum* restores lipid metabolism in triton WR-1339-induced hyperlipidemic mice and prevents lipoprotein-rich plasma oxidation," *Food Sci. Human Wellness*, 2017;6(1):28–33.
5. Basil NI. Antioxidant Activity of *Cnestis ferruginea* and *Uvaria chamae* Seed Extracts. *Brit. J. Pharm. Res*, 2017;16(1):1-8.
6. Kone M, Toure A, Ouattara K, Coulibaly A. Phytochemical Composition, Antioxidant and Antibacterial Activities of Root of *Uvaria chamae* P. Beauv. (Annonaceae) Used in Treatment of Dysentery in North of Côte d'Ivoire. *Intl. J. Pharm. Phytochem. Res.* 2015;7(6):1047-1053.
7. Awodiran MO, Adepiti AO, Akinwunmi KF. Assessment of the cytotoxicity and genotoxicity properties of *Uvaria chamae* P. Beauv (Annonaceae) and *Morinda lucida* Benth (Rubiaceae) in mice. *Drug and chem. Toxicol.* 2017;20-45.
8. Madubunyi, II. Hepatoprotective activity of *Uvaria chamae* root bark methanol extract against acetaminophen-induced liver lesions in rats. *Comp Clin Pathol.* 2012;21:127–135. Available: <https://doi.org/10.1007/s00580-010-1072-8>
9. NIH Guide. Revised Guide for the Care and use of Laboratory Animals. 1996;(25):28.
10. Al-Hashem F, Dallak M, Bashir N, Abbas M, Elessa R, Khalil M, Al-Khateeb, M. Camel's milk protects against cadmium chloride-induced toxicity in white albino rats, *Am. J. Pharmacol. Toxicol.* 2009;4:107
11. Reitman S, Frankel S. Colorimetric methods for aspartate and alanine aminotransferase. *Am J Clin Path.* 1957;28(1):55-60.

- DOI:10.1093/ajcp/28.1.56] [PMID]
12. Satoh K. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. *Clinica Chimica Acta*. 1978;90(1):37-43.
DOI:10.1016/0009-8981(78)90081-5] [PMID]
 13. Aebi H. Catalase *In vitro*. *Methods enzymol*. 1984;105:121-6.
DOI:10.1016/S0076-6879(84)05016-3
 14. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. *Clin Chem*. 1974;20(4):470-5.
DOI:10.1093/clinchem/20.4.470
 15. Fossati P, Prencipe L. Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin Chem*. 1982;28(10):2077-80.
DOI:10.1093/clinchem/28.10.2077
 16. Burstein M, Scholnick HR, Morfin R. Rapid method for the isolation of lipoproteins from human serum by precipitation with polyanions. *J Lipid Res*. 1970;11(6):583-95.
DOI:10.1016/S0022-2275(20)42943-8
 17. Rao S, Snaith A, Marino D. et al. Tumour-derived alkaline phosphatase regulates tumour growth, epithelial plasticity and disease-free survival in metastatic prostate cancer. *Br. J. Cancer*. 2017;116:227–236. Available:https://doi.org/10.1038/bjc.2016.402
 18. Champe PC, Havey RA. Cholesterol metabolism. In: Lippincott's illustrated reviews biochemistry. 2nd edition. Champe PC, Havey RA.(eds). JB Lippincott, Kendallville. 1994;210-225.
 19. Ehiaghe FA. Some physiochemical changes associated with type 2 diabetes mellitus in Benin City, Nigeria. *Intl J. Biol. Chem. Sci*. 2015;9(5):2582–2588.
DOI: http://dx.doi.org/10.4314/ijbcs.v9i5.27
 20. Niedworok E, Bielaszka A. Comparison of the effect of vitamins A and E on aging processes of edible vegetable oils. *Pol. J. Envi. Stud*. 2007;16:861-865.
 21. Miaffo D, Wansi SL, Mbiantcha M, Poualeu SL, Guessom OK, Nchouwet LM, Kamanyi A. Toxicological Evaluation of Aqueous and Acetone Extracts of *Combretum molle* Twigs in Wistar Rats. *Elect. J. Biol*. 2015;11.
 22. Gardner R, Salvador A, Moradas-Ferreira P. Why does SOD overexpression sometimes enhance, sometimes decrease, hydrogen peroxide production? A minimalist explanation. *Free Radic. Biol. Med*. 2002;32:1351-1357.
 23. de Haan JB, Bladier C, Griffiths P, Kelner M, O'Shea RD, Cheung NS, Bronson RT, Silvestro MJ, Wild S, Zheng SS, Beart PM, Hertzog PJ, Kola I. Mice with a homozygous null mutation for the most abundant glutathione peroxidase, Gpx1, show increased susceptibility to the oxidative stress-inducing agent's paraquat and hydrogen peroxide. *J Biol Chem*. 1998;273:22528–22536.
Available:https://doi.org/10.1074/jbc.273.3.22528
 24. Nwobodo EI, Nwosu DC, Ogbodo SO, Ugwuene FO, Ihim AC, Abi NO. Evaluation of Antilipid Peroxidation and Hypolipidemic Potentials of *Azadirachta indica* Leaf Aqueous Extract in Paracetamol Induced Hepatotoxicity in Wistar Rats. *Intl. J. Infor. Resol.Revolu*. 2018;4(2): 3615-3619.
 25. Cuypers A, Plusquin M, Remans T, Jozefczak M, Keunen E, Gielen H. Cadmium stress: an oxidative challenge. *Biometals*. 2010; 23:927–40.
Available:https://doi.org/10.1007/s10534-010-9329-x
 26. Arroyo VS, Flores KM, Ortiz LB, Gómez-Quiroz LE, Gutiérrez-Ruiz MC. Liver and Cadmium Toxicity. *J Drug MetabToxicol*. 2012;S5:001.
DOI: 10.4172/2157-7609.S5-001
 27. Satarug S, Garrett SH, Sens MA, Sens DA. Cadmium, environmental exposure, and health outcomes. *Envir. Healt. Perspect*. 2010;118(2):182–190.
Available:https://doi.org/10.1289/ehp.0901234
 28. Asagba SO. Biochemical changes in urine and plasma of Rats in food_chain mediated cadmium toxicity. *Nig.J.Biochem. Biol*. 2010;25(1):9-17.
Available:http://dx.doi.org/10.1177/0748233710371108
 29. Yakubu MT, Akanji MA, Oladiji AT. Effects of oral administration of aqueous extract of *Fadogiaagrestis* (Schweinf. Ex Hiern) stem from some testicular function indices of male rats. *J Ethnopharmacol*. 2008; 115(2):288-92.

- DOI: 10.1016/j.jep.2007.10.004.
30. Panagiotakos B, Pitsavos C, Skoumas J, Chrysohoou C, Toutouza M, Stefanadis, C.I. Importance of LDL/HDL ratio as a predictor for coronary heart disease events in patients with heterozygous familial hypercholesterolemia: A 15-year follow-up (1987-2002). *Curr Med Res Opin.* 2003; 19:89–94.
DOI:10.1016/s0002-8703(03)00442

© 2022 Njoku et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

*The peer review history for this paper can be accessed here:
<https://www.sdiarticle5.com/review-history/86667>*