

Research Article

Kigelia africana Synthesized Gold Nanoparticles Attenuates Cadmium-Induced Hepatotoxicity in Rats

Emmanuel N. Uhwo¹, Ngozi K. Achi¹, Chiemeziem A. Obike¹, Jacenta C. Ukpabo-Ugo¹, Parker E. Joshua², Jude C. Ogotu¹

¹Department of Biochemistry, College of Natural Sciences, Michael Okpara University of Agriculture, Umudike, Nigeria

²Department of Biochemistry, University of Nigeria Nsukka, Nigeria

OPEN ACCESS

*CORRESPONDENCE

Uhwo, E. N.
uhwo.emmanuel@mouau.edu.ng
+234-806-734-6144

ARTICLE HISTORY

Received: 17/04/2025
Reviewed: 28/08/2025
Revised: 10/09/2025
Accepted: 13/10/2025
Published: 30/01/2026

CITATION

Uhwo E. N., Achi N. K., Ukpabi J. C., Joshua P. E. and Ogotu J. C. (2025). *Kigelia africana* synthesized gold nanoparticles attenuates cadmium-induced hepatotoxicity in rats *Nigerian Journal of Biochemistry and Molecular Biology*. 40(2), 191-201
<https://doi.org/10.4314/njbmb.v40i2.9>

ABSTRACT

Cadmium (Cd) exposure induces liver damage by promoting oxidative stress and inflammation. *K. africana*-synthesized gold nanoparticles (Ka-AuNPs) have the ability to inhibit the process. The research aimed to investigate the protective effects of *K. africana* synthesized gold nanoparticles (Ka-AuNPs) against hepatotoxicity in rats. Thirty male Wistar rats were randomly divided into six groups (n = 5). Group I served as the control, group II received 10 mg/kg b.wt of Ka-AuNPs only, and groups III, IV, V, and VI were orally administered 20 mg/kg b.wt of cadmium chloride (CdCl₂) for seven consecutive days. Groups IV, V, and VI received 10 mg/kg b.wt of silymarin and 5 and 10 mg/kg b.wt of Ka-AuNPs, respectively, over a period of 21 days. Subsequently, liver function markers: alanine transaminase (ALT), aspartate transaminase (AST), liver arginase, and γ -glutamyl transferase (GGT) activities were assessed. Malondialdehyde, blood albumin level, superoxide dismutase (SOD), and catalase activities were determined, followed by histological examination of the hepatic tissue. Administration of CdCl₂ orally caused a significant (p<0.05) increase in alanine transaminase (ALT), aspartate transaminase (AST), liver arginase, and γ -glutamyl transferase (GGT) activities in group III compared with the normal control. Similarly, malondialdehyde level increased significantly (p<0.05) in Cd-intoxicated rats compared with the normal control. Conversely, the administration of 10 mg/kg b.wt. of silymarin and Ka-AuNPs led to a significant (p<0.05) reduction in MDA levels, ALT, AST, hepatic arginase, and GGT activities in the treatment groups compared to the CdCl₂-exposed group. Additionally, increased blood albumin levels and superoxide dismutase and catalase activities were observed in the treated groups relative to the untreated CdCl₂-exposed rats. Histological examination revealed moderate to normal hepatic architecture in the treated groups against CdCl₂-exposed rats without treatment. It may be inferred that *K. africana*-synthesized gold nanoparticles alleviated hepatic toxicity caused by cadmium exposure.

Keywords: Cadmium; *K.africana*; Gold nanoparticles; Hepatotoxicity; Antioxidant.

INTRODUCTION

Cadmium (Cd) is a toxic environmental contaminant resulting from industrial and agricultural activities. Bioaccumulation in the environment—encompassing the atmosphere, soil, and water—poses a threat to human health, potentially resulting in anaemia, hepatocellular damage, osteoporosis, and carcinogenic effects through oxidative stress (Chowdhury *et al.*, 2024., Momeni *et al.*,

2020). The toxicity of Cd mostly arises from the indirect generation of free radicals, although it is also associated with lipid peroxidation, apoptosis, alterations in protein structure, and DNA damage. These pathways may cause oxidative damage to vital organelles by exceeding the antioxidant defence system, interacting with Fenton metals, and other bioelements that produce free radicals (Joardar *et al.*, 2019., Momeni *et al.*, 2020., Qu *et al.*, 2024). Liver damage marked by hepatocellular necrosis, caused by

Copyright © 2025 Uhwo *et al.* This is an open access article distributed under the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/) CC BY 4.0, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

exposure to heavy metals like cadmium, results in excessive formation of reactive oxygen species (ROS) in hepatocytes due to oxidative stress, culminating in the covalent attachment of radicals to several proteins (Teschke, 2022). The accumulation of Cd predominantly in the liver and kidneys, accounts for approximately 75% of the total cellular concentration (Poosa and Vanapatla, 2020). Studies demonstrate that the ingestion of Cd, even at a minimal concentration of 10 mg/L in potable water, leads to liver damage (Chowdhury *et al.*, 2024). The respiratory system is the principal entrance pathway for Cd, with the gastrointestinal tract serving as a secondary route, whereas dermal absorption is rather rare. Upon exposure, Cd is conveyed into the bloodstream by erythrocytes and albumin, subsequently accumulating in the kidneys (Satarug, 2024), liver, and gastrointestinal system (Tinkov *et al.*, 2018). Cd elimination from the body occurs gradually via the kidneys, urine, saliva, and lactation-related milk (Genchi *et al.*, 2020). Cd accumulates in flora and wildlife, demonstrating a prolonged half-life of around 25 to 30 years (Asli and Bedriye, 2020). The elimination of ingested Cd from the body primarily transpires via urine. The excretion rate is negligible, perhaps attributable to Cd robust affinity for metallothionein (MMTN), which is predominantly reabsorbed in the renal tubules. The human body has a limited ability to respond to cadmium exposure, as the metal does not biologically breakdown into less toxic forms and is removed ineffectively (Peana *et al.*, 2022).

Prolonged contact with cadmium (through air, water, soil, and food) leads to cancer and toxicity to organ systems such as skeletal, urinary, reproductive, cardiovascular, central and peripheral nervous and respiratory systems (Rafati *et al.*, 2017). It has been revealed that human contact with Cd can result in a variety of harms such as renal and hepatic dysfunctions, pulmonary oedema, testicular damage, osteomalacia, and damage to the adrenals and haematopoietic system (Yang *et al.*, 2025).

Experimental data and epidemiological studies indicate that chronic cadmium exposure in humans may be associated with carcinogenesis, mostly impacting the lungs, along with the prostate, kidneys, breast, urinary bladder, nasopharynx, pancreas, and haematopoietic system (Charkiewicz *et al.*, 2023). A direct correlation has been established between Cd exposure and coronary heart disease, stroke, peripheral artery disease, and atherogenic lipid alteration (Hung-Chen *et al.*, 2023). Apoptotic or necrotic events are additional cytotoxic effects of cadmium to a proven human carcinogen (group I of the International Agency for Research on Cancer classification) (Charkiewicz *et al.*, 2023). Victims of cadmium poisoning required urgent gastrointestinal tract irrigation, supportive care, and chemical decontamination chelation therapy of traditional-based with corresponding active chelating agents and nanoparticle-based antidotes (Tinkov *et al.*, 2018). Despite these approaches, more proactive measures with high specificity and accuracy are required.

Nanoscience has just arisen as a new field within science and technology. This is regarded as an assessment of the fundamental characteristics of nanoscale entities (Bayda *et al.*, 2019, Khan *et al.*, 2022). Nanotechnology is a burgeoning field with applications in science and technology centered on the synthesis of innovative materials at the nanoscale. Discoveries in nanoscience have been realized in nanotechnology via the creation of innovative materials and functional systems (Varghese *et al.*, 2019). Nanometer-sized particles exhibit unique features relative to their macroscopic counterparts owing to their increased surface-to-volume ratio. As a result, these nanoparticles have attracted considerable scientific interest in recent years (Altammar, 2023, Malik *et al.*, 2023). The biomedical applications of AuNPs have become a prominent area of research in recent years (Milan *et al.*, 2022, Anik *et al.*, 2022). A significant volume of research has concentrated on the synthesis, stabilization, and fictionalization of AuNPs (Nurakhmetova *et al.*, 2020).

The synthesis and characterization of nanoparticles is a significant area of modern study, as the selection of nanoparticle size and morphology enables precise control of their characteristics and therapeutic uses. The current chemical methods employed for nanoparticle synthesis are energy-intensive and include toxic compounds that produce hazardous waste, making them inappropriate for biological applications. Sputter deposition and thin films, as physical techniques for nanoparticle fabrication, are often difficult to execute.

Consequently, there is an increase need for biocompatible, non-toxic, cost-effective, and environmentally sustainable processes for the synthesis of gold nanoparticles (AuNPs). The current emphasis on the synthesis of AuNPs pertains to the capacity to modify their properties to improve biological interactions. To enhance the biocompatibility of AuNPs, it is recommended to employ non-toxic agents during synthesis. Numerous reducing agents have been recorded in the literature, with sodium borohydride and sodium citrate being the most common (Dheyab *et al.*, 2022). Furthermore, the synthesis of AuNP requires protective agents to prevent reactions with the newly generated particles. Thus, the architecture of AuNPs can be modulated through the application of appropriate techniques and synthesis conditions. These factors resulted in several recommendations for an innovative synthesis process for AuNPs, employing environmentally friendly reduction and protection agents (Miu *et al.*, 2022, Oueslati *et al.*, 2020). Plants function as the principal source of reducing and stabilizing agents, encompassing algae, bacteria, and fungi (Hano *et al.*, 2021, Zuhrotun *et al.*, 2023). Numerous studies have examined the synthesis of nanoparticles using plant extracts, resulting in nanoparticles with sizes ranging from 1.7 nm to 50 nm (Ahmad *et al.*, 2022, Kazemi *et al.*, 2023). Nanomaterials¹ have several applications across various industries (Maha *et al.*, 2023). A multitude of biomedical applications for noble metal nanoparticles has been utilized, producing significant outcomes in a recent

investigation (Yaqoob *et al.*, 2020). AuNPs are employed in the treatment of several diseases owing to their optical, chemical, and biological characteristics (Dheyab *et al.*, 2022).

In many rural areas of Nigeria, especially in isolated settlements in the eastern region, the limited availability of modern medication necessitates the exclusive use of medicinal plants for the treatment of various health conditions. Most local therapies employ the *Kigelia africana* (Lam.) Benth (Family: Bignoniaceae) plant, incorporating its leaves, bark, fruit, or roots. The amalgamation of two or more elements is often utilized, depending on the desired objective. The involvement of all elements in the technique bolsters its credibility and makes it more reliable than other botanical materials in the area. The medicinal properties of *K. africana* can be attributed to its intrinsic phytochemical compounds across many types. *K. africana* is frequently employed in African herbal medicine to treat several ailments, including rheumatism, snakebites, syphilis, and malevolent spirits (Nabatanzi *et al.*, 2020). Phytochemical research has found around 145 compounds extracted from different plant parts, exhibiting anti-inflammatory, antioxidant, antibacterial, antidiabetic, antineoplastic, and anti-urolithic activities (Uhuo *et al.*, 2019, Abbas *et al.*, 2023). The n-hexane leaf extract of *K. africana* exhibited the greatest activity against *P. vulgaris* (6 mm) and the least efficacy against *S. aureus* (2 mm). The bark of *K. africana*, extracted with several solvents, showed susceptibility to *Escherichia coli* and had limited antibacterial efficacy against *K. pneumonia* (Assanti *et al.*, 2020). The aqueous leaf extract of this plant has antidiarrheal effects (Nabatanzi *et al.*, 2020). *K. africana* is commonly employed in Southeastern Nigeria for the treatment of hyperprolactinemia and related conditions (Uhuo *et al.*, 2023). The bioconstituents of herbs, especially phenolics, are attracting increased attention in the food and beverage industry for their ability to improve food quality and nutritional value. Phytochemicals found in medicinal plants are employed as hepatoprotective agents.

Silymarin is a polyphenolic flavonoid derived from *Silybum marianum*. It consists of three phytochemicals (silybin, silidianin, and silicristin) and has a historical precedent as a herbal remedy. Silymarin is a phytotherapeutic compound demonstrating cytoprotective effects due to its antioxidant characteristics and radical scavenging potential (Uhuo *et al.*, 2025). Pharmacological studies indicate that silymarin is a safe herbal compound, with appropriate dosages being non-toxic unless therapeutic levels are misapplied (Mehdi *et al.*, 2023). This study seeks to evaluate the effectiveness of *K. africana* synthesized gold nanoparticles (*Ka*-AuNPs) in alleviating cadmium-induced hepatic injury in a rat model, employing silymarin as a standard hepatoprotective agent.

MATERIALS AND METHODS

Chemical and reagents

Tetrachloroauric acid ($\text{HAuCl}_4 \cdot 3\text{H}_2\text{O}$), sodium phosphate buffer, sodium hydroxide (NaOH), dimethyl sulfoxide (DMSO), bicinchoninic acid protein assay kit, bovine serum albumin (BSA), H_2O_2 (hydrogen peroxide), and nitric acid (HNO_3) were obtained from Sigma-Aldrich (St. Louis, MO, USA). alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (γ -GT) assay kits were obtained from Randox Laboratories Ltd. (55 Diamond Road, Crumlin, County Antrim, BT29 4QY, United Kingdom).

Plant materials

The leaves of *K. africana* were obtained from a farm located in Umuezeoka, Ezza-North LGA, Ebonyi State, Southeast Nigeria. *K. africana* was authenticated by a taxonomist with a voucher specimen number *UBH-K364*, which was kept for referral purposes at the department of Plant Science and Biotechnology herbarium, Michael Okpara University of Agriculture, Umudike. Tap water was used to wash the leaves, dried at room temperature in the laboratory, milled, and weighed for further use.

Biosynthesis of *K. africana* gold nanoparticles (*Ka*-AuNPs)

Kigelia africana gold nanoparticles (*Ka*-AuNPs) were synthesized following the method reported by Adewale *et al.* (2023). Briefly, 10 ml of freeze-dried sample (containing 10 g aqueous extract + 100 mL distilled water) was added to an aqueous solution of 1 mM gold (III) chloride trihydrate (190 mL) on a hot magnetic stirrer at 60 °C for 10 min. The resulting solution was centrifuged at 15,000×g for 15 min and washed twice with distilled water to remove excess plant material. The resulting pellet was air-dried at 25 °C and stored in a refrigerator (4 °C) until further use.

Animal study

Thirty male Wistar rats, mean weight: 100±0.35g were provided by the Animal Unit, Department of Zoology and Environmental Science, University of Nigeria, Nsukka. The rats were kept safe in iron cages under standard conditions of a 12 hour dark-light cycle for 7 days with free access to drinking water and standard pellet feed before induction, which was in line with the approval of the Ethics Committee (Reference number: *MOUAU/BCH/EC/2024/4*).

Experimental design

The animals were grouped into 6 (n = 5) as follows: I normal rats administered daily 0.5 mL of distilled water; II, received 10 mg/kg b.wt of *Ka*-AuNPs; III÷Cd only; IV÷Cd+10 mg/kg b.wt of silymarin; V÷Cd÷ 5 mg/kg b.wt of *Ka*-AuNPs; and VI÷Cd+10 mg/kg b.wt of *Ka*-AuNPs. CdCl_2 (20 mg/kg b.wt) was orally administered to rats for seven days as adopted by Adewale *et al.* (2023). Thereafter, a hepatoprotective drug

(silymarin, 10 mg/kg b.wt) and *Ka*-AuNPs (5 and 10 mg/kg b.wt) were orally administered daily for 21 days.

Preparation of serum and tissues

Blood samples were collected through cardiac puncture under anesthesia and transferred into sample-labeled bottles (Plain and EDTA) while the heart was still beating. Plasma obtained through centrifugation of whole blood was employed for the enzyme assays. Samples in plain bottles were preserved for some times to guarantee adequate coagulation and centrifuged (Model SM800B, Surgifriend Medicals, Essex, England) at 1000 rpm for 15 minutes. The sera obtained were employed to evaluate biochemical indices. Rats were quickly dissected, and their livers were extracted and preserved with ice-cold 0.25 M sucrose solution for histopathological investigation.

Biochemical analysis

Serum liver marker enzymes status

Biochemical analyses included the measurement of alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (γ -GT) activities, and serum albumin concentrations. These parameters were determined using commercially available test kits and products from Randox Laboratories (Crumlin, United Kingdom). The tissue arginase activity was measured using the method described by Hrabák *et al.* (2008).

Determination of malondialdehyde (MDA) level

Malondialdehyde level was assessed with the Varshey and Kale methodology (Varshey *et al.* (1990). In summary, 0.1 ml of sample, 0.9 ml of distilled water, 0.5 ml of 25 % trichloroacetic acid (TCA) and 0.5 ml of 17 % Thiobarbituric acid (TBA) in 0.3 % NaOH were placed into test tubes. The incubation of the contents in the test tube was done for 40 min at 95 °C and then cooled in water. Subsequently, 0.1 ml of 20 % sodium dodecyl sulphate was included into the mixture. The absorbance of the mixture was measured at 600 nm relative to a blank.

Activity of superoxide dismutase (SOD)

The enzyme activity was calculated by the procedure outlined by Xin *et al.* (1991). In summary, 0.1 ml of the sample was mixed with 0.9 ml of distilled water and put into test tubes. Subsequently, 0.1 ml of this mixture was added to 0.9 ml of carbonate buffer, and 75 μ l of xanthine oxidase. The absorbance was measured at 500 nm for 3 minutes at 20-second intervals. The rate of absorbance variations was employed to calculate the enzyme activity.

Measurement of catalase (CAT) activity

Method of Aebi as was reported by Uhuo *et al.* (2025) was adopted for the determination of catalase activity. Shortly, 2.0 ml of H₂O₂, 2.5 ml of phosphate buffer, and 0.5 ml of sample were added into the test tube labeled stock. Volume,

1.0 ml portion of the reaction from the stock test tube was added to the separate test tube and 2 ml of dichromate acetic acid reagent. The absorbance of the mixture was taken at 340 nm in a minute interval for four consecutive times.

Histopathological examination

Tissues were preserved in 10% formalin, embedded in paraffin blocks, and sectioned to a thickness of 5 μ m (Canene-Adams *et al.*, 2013). Hematoxylin-eosin staining was conducted on the slides. Slides were analyzed using a light microscope (OPTIKAB-150, Ponteranica, Italy) equipped with a digital camera.

Statistical analysis

Data are shown as mean \pm SD and were analyzed using Microsoft Excel with one-way analysis of variance (ANOVA) ($p < 0.05$).

RESULTS AND DISCUSSION

Effect of *Ka*-AuNPs on serum ALT activity

The effect of *K. africana* synthesized gold nanoparticles (*Ka*-AuNPs) on ALT is shown in **Fig. 1A**. Alteration in the serum ALT activity induced by cadmium was investigated. Oral administration of 20 mg/kg b.wt of CdCl₂ caused liver damage, evidenced by a significant ($p < 0.05$) elevation in the plasma alanine transaminase (ALT) activity (**Fig. 1A**) in group 3 relative to the normal control group. Pretreatment with *Ka*-AuNPs at 5, 10, and 10 mg/kg b.wt of silymarin led to a substantial ($p < 0.05$) increase in the activity of this marker against CdCl₂-induced only. A non-significant ($p > 0.05$) increase in ALT activity in normal rats treated with 10 mg/kg of *Ka*-AuNPs (group 2) was recorded when compared with normal control rats.

Effect of *Ka*-AuNPs on serum AST activity

The impact of *Ka*-AuNPs on serum AST activity is illustrated in **Fig. 1B** demonstrating their effect in CdCl₂-induced hepatotoxicity in rats. Significant ($p < 0.05$) elevation of AST activity was recorded with CdCl₂ only compared to the normal control rats. In contrast, AST activity decreased considerably ($p < 0.05$) in CdCl₂-intoxicated rats treated with 10 mg/kg b.wt. of silymarin and 10 mg/kg b.wt of *Ka*-AuNPs compared to CdCl₂ only. Similarly, the concentration of AST was reduced substantially ($p < 0.05$) in CdCl₂-intoxicated rats administered 10 mg/kg b.wt of *Ka*-AuNPs compared to those treated with 5 mg/kg b.wt of *Ka*-AuNPs. Non-significant ($p > 0.05$) increase in AST activity was detected in the rats treated with 10 mg/kg of *Ka*-AuNPs (group 2) when compared with the normal control.

Effect of *Ka*-AuNPs on serum albumin level

Fig. 1D depicts the effect of *Ka*-AuNPs on serum albumin levels in CdCl₂-induced hepatotoxicity. A notable ($p < 0.05$) reduction in serum albumin level was seen in CdCl₂ only rats relative to CdCl₂-intoxicated rats treated with 10 mg/kg b.wt of *Ka*-AuNPs and normal rats receiving 10 mg/kg b.wt of *Ka*-AuNPs. A remarkable ($p < 0.05$) increase in serum albumin

levels was observed in rats treated with 10 mg/kg b.wt of *Ka*-AuNPs in contrast to CdCl₂-intoxicated rats receiving 5 and 10 mg/kg b.wt of *Ka*-AuNPs, respectively. Similarly, a significant ($p < 0.05$) increase in serum albumin level was observed in Cd + 10 mg/kg b.wt of silymarin compared with the CdCl₂-intoxicated rats treated with 5 and 10 mg/kg b.wt of *Ka*-AuNPs, respectively.

Effect of *Ka*-AuNPs on the activity of liver arginase

The inhibitory effect of *Ka*-AuNPs on the activity of liver arginase in CdCl₂-induced hepatotoxicity is presented in Fig. 1C. A notable ($p < 0.05$) increase in arginase activity was recorded in CdCl₂-treated rats relative to that in normal control rats. A non-significant ($p > 0.05$) increase was observed in the activity of arginase in rats receiving 10 mg/kg b.wt of *Ka*-AuNPs (group 2) in comparison with the normal control. There was a substantial ($p < 0.05$) reduction in arginase activity in Cd+silymarin group relative to CdCl₂-induced rats treated with 5 and 10 mg/kg b. wt of *Ka*-AuNPs, respectively, and a dose-dependent reduction of arginase activity was observed in Cd + 10 mg/kg b. wt of *Ka*-AuNPs against group v (Cd + 5 mg/kg b.wt of *Ka*-AuNPs).

Effect of *Ka*-AuNPs on MDA level

Fig. 2A illustrates the impact of *Ka*-AuNPs on MDA levels in CdCl₂-induced liver injury in rats. A statistically remarkable ($p < 0.05$) elevation in MDA levels was recorded in rats intoxicated with CdCl₂ compared to the control. A non-significant ($p > 0.05$) decrease in MDA levels was noted in Cd+ 10 mg/kg b.wt of *Ka*-AuNPs compared with Cd+10 mg/kg b.wt of silymarin and Cd + 5 mg/kg b.wt of *Ka*-AuNPs. Group II administered 10 mg/kg b.wt of *Ka*-AuNPs exhibited statistically a non-significant ($p > 0.05$) increases in MDA levels relative to the normal control.

Inhibition of SOD activity by *Ka*-AuNPs

Fig. 2B depicts the effect of *Ka*-AuNPs on superoxide dismutase (SOD) activity. A significant ($p < 0.05$) reduction in SOD activity was noted in rats exposed to Cadmium relative to the control group. CdCl₂-induced rats treated with 10 mg/kg b.wt of *Ka*-AuNPs demonstrated a non-significant ($p > 0.05$) elevation in SOD activity relative to those intoxicated rats administered 10 mg/kg b.wt of silymarin. Variations in SOD activity were observed between CdCl₂-intoxicated rats treated with 5 and 10 mg/kg b.wt of *Ka*-AuNPs, respectively. A reduction in SOD activity was recorded in normal rats administered 10 mg/kg b.wt of *Ka*-AuNPs compared with the normal control.

Effects of *Ka*-AuNPs on Catalase activity

Catalase activity is shown in Fig. 2C. The activity of catalase was not significantly ($p > 0.05$) reduced in the group 2 relative to the normal control group. The test group treated with silymarin (10 mg/kg b.wt) demonstrated a substantial ($p < 0.05$) elevation in CAT activity relative to rats administered 10 mg/kg b. wt of *Ka*-AuNPs and CdCl₂-intoxicated rats treated with 5 and 10 mg/kg b.wt of *Ka*-

AuNPs, respectively. In contrast, group administered 10mg/kg b.wt of *Ka*-AuNPs demonstrated statistical a non-significant ($p > 0.05$) increase in catalase activity against the group which received 5 mg/kg b.wt of *Ka*-AuNPs.

Effects of *Ka*-AuNPs on γ -glutamyl transferase (GGT) activity

Fig.2D depicts the activity of γ -glutamyl transferase. A significant ($p < 0.05$) increase in γ -glutamyl transferase activity was noted in CdCl₂-intoxicated rats relative to rats treated with 10 mg/kg b.wt of *Ka*-AuNPs. Furthermore, there were non notable variations in the activity of GGT between the Cd+10 mg/kg b.wt of *Ka*-AuNPs and 5 mg/kg b.wt of *Ka*-AuNPs groups. The group treated with silymarin (Cd+10 mg/kg b.wt of silymarin) demonstrated a significant ($p < 0.05$) increase in GGT activity compared with the rats administered 10 mg/kg b.wt of *Ka*-AuNPs.

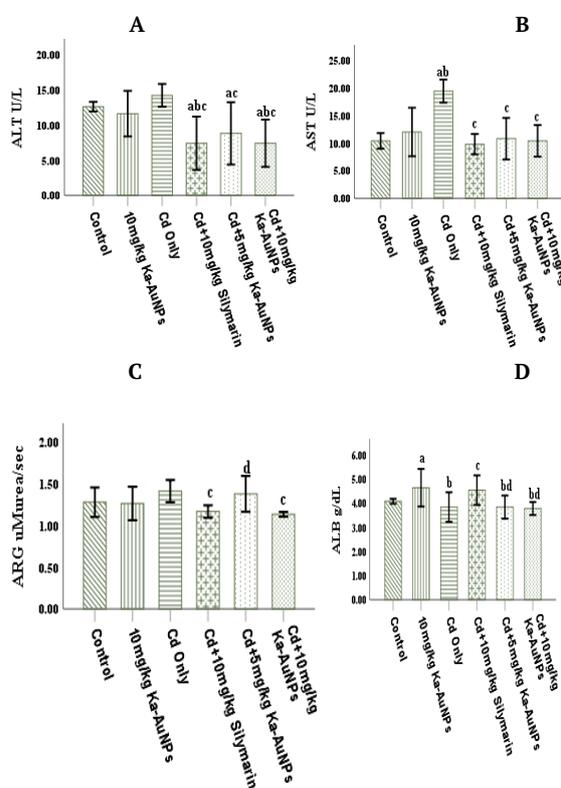
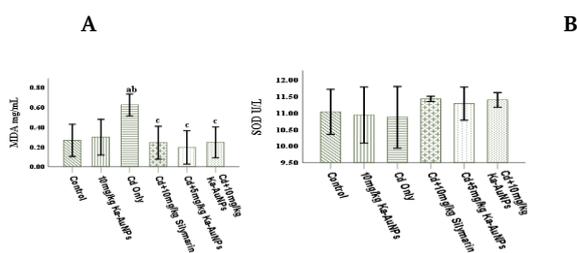


Fig.1 A, B C and D represent the effects of *Ka*-AuNPs on ALT, AST, liver Arginase and serum Albumin levels in the different experimental groups. Values are mean \pm SD, n = 5. ^a $p < 0.05$ vs group1, ^b $p < 0.05$ vs group2, ^c $p < 0.05$ vs group3, ^d $p < 0.05$ vs group4.



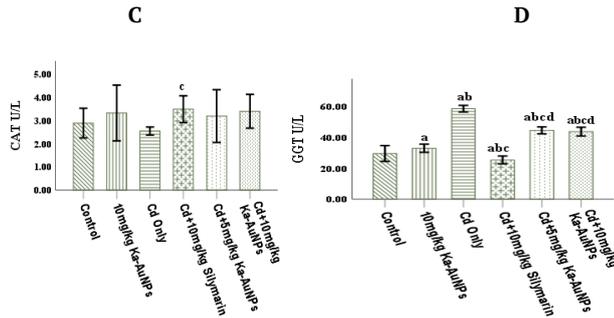


Fig.2 A, B,C and D represent the effects *Ka-AuNPs* on MDA, SOD, CAT, GGT, levels in the different experimental groups. Values are mean±SD, n = 5. ^ap<0.05 vs group1, ^bp<0.05 vs group2, ^cp<0.05 vs group3, ^dp<0.05 vs group 4.

Histopathological examination

Fig. 3A showed a normal histomorphology of the liver with normal hepatocytes arranged in interconnecting cords around the central veins (V). Normal structures in the portal areas (P) were also observed. In Fig.3B, mild-to-moderate hepatocellular carcinoma is presented. Affected hepatocytes appeared mildly swollen and contained clear cytoplasmic vacuoles. Fig.3C presents severe hepatocellular damage. Affected hepatocytes appear swollen with clear cytoplasmic vacuoles (arrow), Central vein (V), portal area (P). Moderate to marked periportal infiltration of mononuclear inflammatory leukocytes with piecemeal necrosis of surrounding hepatocytes (arrow) was observed. Liver sections in fig.6 showed mild to moderate hepatocellular swelling with clear cytoplasmic vacuoles (arrow). Moderate periportal infiltration of mononuclear inflammatory leukocytes with piecemeal necrosis was observed. Similarly, Fig.3E presented diffuse, moderate hepatocellular swelling. Affected hepatocytes appear swollen with clear cytoplasmic vacuoles (arrow). In Fig,3 F liver sections showed diffuse, and mild hepatocellular swelling compared to Fig.3D

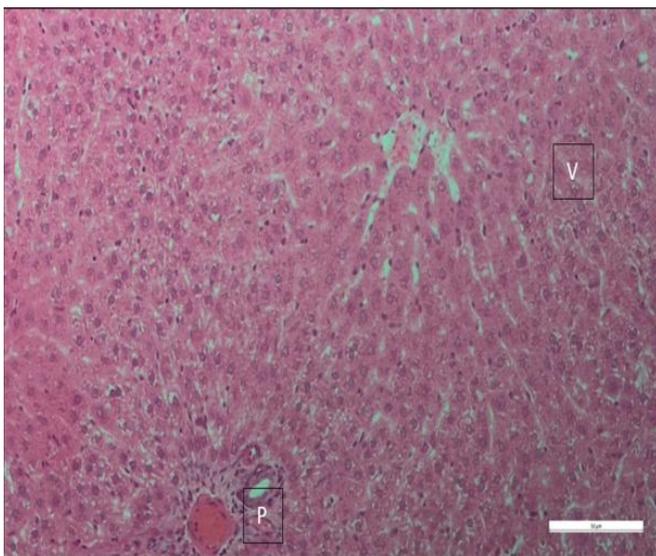


Fig. 3A. Histological section of hepatic tissue of normal rats (Mgf. X200)

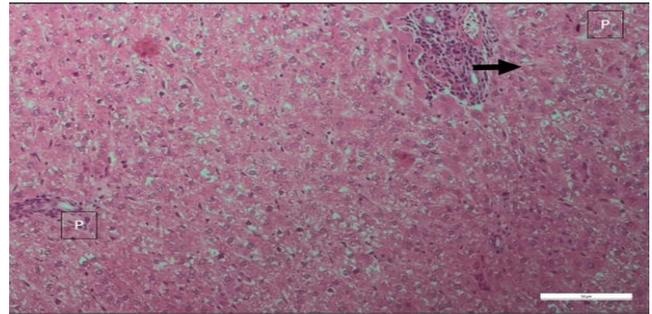


Fig. 3B. Histological section of hepatic tissue of normal + 10mg/kg *Ka-AuNPs* (Mgf. X200)

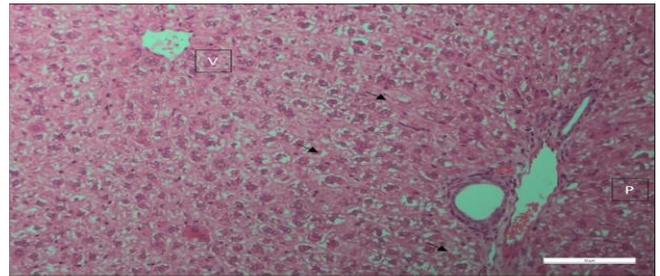


Fig. 3C. Histological section of hepatic tissue of Cd-induced only (Mgf. X200)

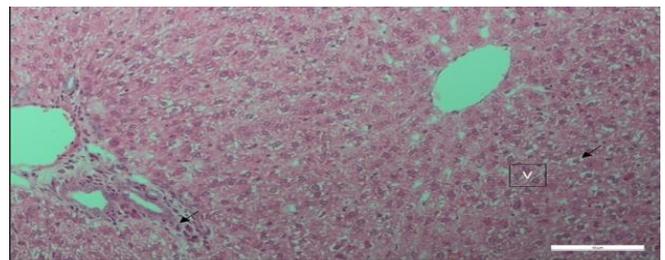


Fig. 3D. Histological section of hepatic tissue of Cd-induced + 10mg/kg *silymarin*(Mgf. X200)

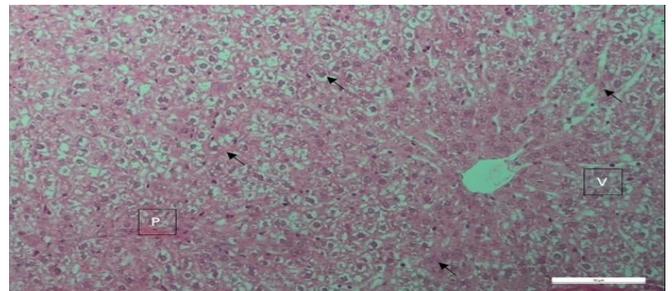


Fig.3E. Histological section of hepatic tissue of Cd-induced + 5mg/kg *Ka-AuNPs* (Mgf.X200)

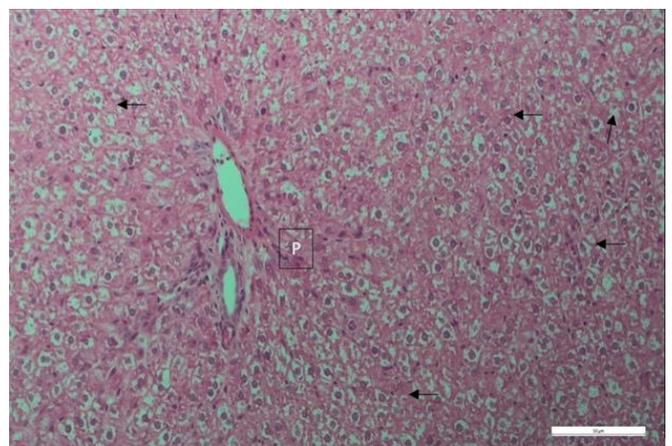


Fig.3F. Histological section of hepatic tissue of Cd-induced + 10mg/kg *Ka-AuNPs* (Mgf.X200)

Discussion

Cadmium is a toxic metal widely employed in various industries. Cadmium exposure induces oxidative stress by its accumulation in some tissues, which is the principal mechanism responsible for severe clinical disorders (Genchi *et al.*, 2020). The harmful effects of cadmium led to increased hepatic enzyme levels (ALT and AST), probably due to altered membrane permeability and consequent enzyme leakage into the bloodstream (Niture *et al.*, 2021). The elevation of serum ALT and AST activity in the Cd-induced group, compared to the normal control, unequivocally signifies the extent of hepatic necrosis, leading to the compromise of cellular architecture and membrane functional integrity. This corresponds with the results of Adefegha *et al.* (2015) and Kaur *et al.* (2020), which demonstrated that hepatotoxicity occurred in rats exposed to CdCl₂. Adewale *et al.* (2020) noted a similar finding. The reduced activity of these enzymes following treated with different doses of *Ka*-AuNPs demonstrated the inhibitory effectiveness of *Ka*-AuNPs against Cd-induced hepatic damage.

Hypoalbuminemia signifies an inflammatory condition resulting from chemical agents or surgical interventions. A decreased serum albumin level signifies the degree of inflammation, which is associated with shortened life expectancy. Variations in blood albumin levels provide significant evidence of either improvement or deterioration in clinical condition. Thus, it can be ascribed to the liver's synthetic deficiency observed by Poosa and Vanapatla (Teschke, 2022) in experimental rats intoxicated with cadmium relative to the control group. The reversal effect was achieved when *Ka*-AuNPs were administered at various doses to Cd-intoxicated rats, in comparison to the untreated Cd-intoxicated group (Fig. 1D). Similarly, increased serum albumin levels were seen following silymarin administration (10 mg/kg) in cadmium-exposed rats compared to the untreated cadmium-exposed group. Silymarin is a phytochemical demonstrating hepatoprotective effects due to its antioxidant characteristics and radical scavenging abilities. The acknowledged pathways through which silymarin provides protective benefits encompass the inhibition and regulation of cellular transporters, p-glycoprotein, oestrogen receptors, and nuclear receptors (Abdoh *et al.*, 2018). Subsequently, preclinical data have shown that silymarin can reduce oxidative stress and consequent cytotoxicity, thereby protecting healthy liver cells orthose that have not yet experienced irreparable damage (Gillessen *et al.*, 2020).

Arginase is a crucial enzyme in the urea cycle, and its activity functions as an important diagnostic signal, as it rapidly escapes from hepatocytes after liver damage (Clemente *et al.*, 2020). The predominant hepatotoxic chemicals damage liver cells by lipid peroxidation and various kinds of oxidative destruction. In Cd-induced cells, elevated arginase activity was seen only in comparison to the treatment groups and normal controls. Furthermore, the diminished arginase levels after treatment with different

doses of *Ka*-AuNPs in Cd-induced hepatotoxicity in experimental subjects, relative to untreated Cd-induced rats, underscore the therapeutic efficacy of the *Ka*-AuNPs.

The elevation of MDA values in this study signifies cadmium toxicity during exposure. Oxidative damage is the principal mechanism via which cadmium exerts its detrimental effects. Hepatocellular damage is linked to inflammation, lipid and protein peroxidation, and the oxidation of biological constituents (Allameh *et al.*, 2023). Cadmium-induced free radicals take electrons from lipid molecules, leading to lipid peroxidation, as seen by the increased levels of MDA in this study. The results demonstrated a decrease in MDA levels and an increase in the activity of antioxidant enzymes (SOD and CAT) in the groups administered the extract, compared to untreated Cd-intoxicated rats. This demonstrates the scavenging capacity of the *Ka*-AuNPs for free radicals, hence diminishing oxidative stress.

Gamma-glutamyl transferase (GGT) is recognized as an enzyme linked to hepatic disorders. Increased GGT synthesis is associated with inflammatory states, and its mRNA expression can be induced by tumor necrosis factor alpha (TNF- α) (Takemura *et al.*, 2021, Xing *et al.*, 2023). The significant increase in GGT concentration noted in this study indicates that cadmium provoked an inflammatory response. The beneficial impact of *Ka*-AuNPs, mostly at a dose of 10 mg/kg b.wt on cadmium-intoxicated rats was confirmed by a reduction in enzyme activity. The significant decrease in GGT levels after extract administration in the test groups compared to the Cd-only group confirms the efficacy of *Ka*-AuNPs, although silymarin exhibited superior performance in this aspect.

The study established the attenuation of cadmium hepatotoxicity by gold nanoparticles synthesized from *K. africana* (*Ka*-AuNPs). This mechanism may result from the inhibition of oxidative damage and the cessation or postponement of lipid peroxidation. The bioconstituents of *K. africana* demonstrate antioxidant capabilities by neutralizing free radicals produced during cadmium exposure. Moreover, the exceptional characteristics of synthesized nanoparticles include their dimensions, which are within the optimal range (10–100 nm) for passive drug delivery systems, facilitating effective permeability and retention effects (Lee *et al.*, 2020). Consequently, the dimensions of the nanoparticles enhance their permeability and retention duration at the target location, so potentially mitigating damage induced by cadmium in the liver. The antioxidant efficacy of *Ka*-AuNPs via the release of surface-capped phytochemicals was distinctly evidenced in the treatment groups compared to the control. Consequently, it can be asserted that *Ka*-AuNPs can mitigate hepatic damage induced by cadmium exposure, as evidenced by the study's findings. Biosynthesized nanoparticles can play a crucial role in clinical applications for drug delivery, owing to their permeability, retention time, and safety profile.

CONCLUSION

Current treatments for liver damage are insufficient and ineffective in clinical practice, prompting researchers to pursue the development of improved therapeutic methods characterized by enhanced specificity, efficacy, and reduced toxicity. The advent of nanoscience has generated optimism for the proper management of life-threatening liver diseases in the near future. Nanoparticles have emerged as optimal choices because of their extended retention period, chelating properties, versatile morphology, and permeability. Biologically synthesized Ka-AuNPs are superior for addressing Cd-induced hepatotoxicity due to its antioxidant potentials. The reduction of liver markers in Cd-induced rats is a confirmatory evidence of this property. Further research is advised to characterize Ka-AuNPs, which will assist in elucidating a precise biochemical mechanism by which it mitigates the detrimental effects of cadmium exposure.

Ethic approval

Protocols of the experiment were approved (MOUAU/BCH/EC/2024/4) by the Animal Ethics Committee.

AUTHORS' CONTRIBUTIONS

ENU: Methodology, Investigation, Formal analysis, Data curation, Writing - original draft, Writing - review & editing. Ngozi Kalu Achi: Supervision, Methodology, Writing - original draft, Writing - review & editing. CAO: Investigation, Formal analysis, Data curation. JCU: Project administration, Conceptualization, PEJ: Writing - original draft, Writing - review & editing. JCO: Investigation, Formal analysis. All authors have read and agreed to publish the revised version of the manuscript.

FUNDING STATEMENT

This study did not receive any grants from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest

ACKNOWLEDGEMENT

Authors are grateful for the analytical support from Shalom Laboratory Services, University of Nigeria Nsukka, Nigeria. Special regard to the staff of Biochemistry Laboratory, Michael Okpara University of Agriculture, Umudike, Nigeria, for the supplementary analysis

List of abbreviations

Cd-Cadmium, CdCl₂. Cadmium chloride, AuNPs-gold nanoparticles, Ka-AuNPs-Kigelia africana synthesized gold nanoparticles, SOD- superoxide dismutase, CAT- catalase, MDA- malondialdehyde, ROS-reactive oxygen species, DMSO-dimethyl sulfoxide, ALT alanine transaminase, AST aspartate transaminase, GGT-γ-glutamyltransferase, MMTN-metallothionein

REFERENCES

- Abbas, Z., Mustafa, S., Khan, M. F., Khan, M. A., Massey, S., Dev, K., Husain, S. A. (2023). Therapeutic importance of *Kigelia africana subsp. africana*: an alternative medicine. *Natural Product Research*, 1–15. <https://doi.org/10.1080/14786419>.
- Adewale, O. B., Anadozie, S. O., Odomene, J. C., Akinlade, O., Adewumi, F. D., Idowu, O. T., & Osukoya, O. A. (2023). Attenuation of cadmium-induced hepatotoxicity by orally administered *Crassocephalum rubens* synthesized gold nanoparticles in rats. *Comparative Clinical Pathology*, 32(4), 691–698. <https://doi.org/10.1007/s00580-023-03477-y>
- Adefegha, S. A., Oyeleye, S. I., & Oboh, G. (2015). Distribution of phenolic contents, antidiabetic potentials, antihypertensive properties, and antioxidative effects of soursop (*Annona muricata* L.) fruit parts in vitro. *Biochemistry Research International*, 2015(1), 347673. doi: 10.1155/2015/347673.
- Adewale OB, Egbeyemi KA, Onwuelu JO, Potts-Johnson SS, Anadozie SO, Fadaka AO, Osukoya OA, Aluko BT, Johnson J, Obafemi TO, & Onasanya A.(2020). Biological synthesis of gold and silver nanoparticles using leaf extracts of *Crassocephalum rubens* and their comparative *in vitro* antioxidant activities. *Heliyon*. 16;6(11):e05501
- Abdoh Taleb, Khalil Ali Ahmad, Awais Ullah Ihsan, Jia Qu, Na Lin, Kamal Hezam, Nirmala Koju, Lei Hui, & Ding Qilong (2018). Antioxidant effects and mechanism of silymarin in oxidative stress induced cardiovascular diseases, *Biomedicine & Pharmacotherapy*, Volume 102, 2018, Pages 689–698, <https://doi.org/10.1016/j.biopha.2018.03.140>.
- Ahmad, B., Chang, L., Satti, U. Q., Rehman, S. U., Arshad, H., Mustafa, G., Shaukat, U., Wang, F., & Tong, C. (2022). Phyto-Synthesis, Characterization, and In Vitro Antibacterial Activity of Silver Nanoparticles Using Various Plant Extracts. *Bioengineering (Basel, Switzerland)*, 9(12),779. <https://doi.org/10.3390/bioengineering9120779>
- Allameh, A.; Niayesh-Mehr, R.; Aliarab, A.; Sebastiani, G.; Pantopoulos, K. (2023). Oxidative Stress in Liver Pathophysiology and Disease. *Antioxidants* 12,1653. <https://doi.org/10.3390/antiox12091653>
- Anik, M. I., Mahmud, N., Al Masud, A., & Hasan, M. (2022). Gold nanoparticles (GNPs) in biomedical and clinical applications: A review. *Nano Select*, 3(4), 792–828.
- Assanti, G., Kaur, R., Nizard, S., Pollack-Blackwood, E., Rafferty, B., Priano, C., Fernández Romero, J. A., & Koroch, A. R. (2022). Biology, chemistry, and pharmacological activity of *Kigelia africana* (Bignoniaceae) and *Garcinia kola* (Clusiaceae) - a review. *Journal of Medicinally Active Plants*, 11(1), 1–21. <https://doi.org/10.7275/hece-wp36>
- Asli Hocaoglu-Ozyigit and Bedriye Nazli Genc (2020). Cadmium in plants, humans and the environment

- Frontiers in Life Sciences and Related Technologies 1(1)12-21
- Altammar K. A. (2023). A review on nanoparticles: characteristics, synthesis, applications, and challenges. *Frontiers in Microbiology*, 14,1155622. <https://doi.org/10.3389/fmicb.2023.1155622>
- Bayda, S., Adeel, M., Tuccinardi, T., Cordani, M., &Rizzolio, F. (2019). The History of Nanoscience and Nanotechnology: From Chemical-Physical Applications to Nano medicine. *Molecules (Basel, Switzerland)*, 25(1),112. <https://doi.org/10.3390/molecules25010112>
- Canene-Adams K (2013). Preparation of formalin-fixed paraffin-embedded tissue for immunohistochemistry. In: Lorsch J, editor. *Methods in enzymology*. Vol. 533. London: Academic Press: 2013. p. 225–233. Chapter 15
- Chowdhury, F. N., & Rahman, M. M. (2024). Source and distribution of heavy metal and their effects on human health. In *Heavy metal toxicity: human health impact and mitigation strategies* (pp. 45-98). Cham: Springer Nature Switzerland.
- Charkiewicz, A.E.; Omeljaniuk, W.J.; Nowak, K.; Garley, M.; Nikliński, J. (2023). Cadmium Toxicity and Health Effects A Brief Summary. *Molecules* 28, 6620. <https://doi.org/10.3390/molecules28186620>
- Charkiewicz, A. E., Omeljaniuk, W. J., Nowak, K., Garley, M., & Nikliński, J. (2023). Cadmium Toxicity and Health Effects-A Brief Summary. *Molecules (Basel, Switzerland)*, 28(18), 6620. <https://doi.org/10.3390/molecules28186620>
- Clemente, S., Gonçalves, Aren van Waarde, Inês F. Antunes, Alexander Dömling, and Philip H. Elsinga. (2020). "Arginase as a Potential Biomarker of Disease Progression: A Molecular Imaging Perspective" *International Journal of Molecular Sciences* 21, no. 15: 5291. <https://doi.org/10.3390/ijms21155291>
- Dheyab, M. A., Aziz, A. A., Moradi Khaniabadi, P., Jameel, M. S., Oladzadabbasabadi, N., Mohammed, S. A., Abdullah, R. S., & Mehrdel, B. (2022). Monodisperse Gold Nanoparticles: A Review on Synthesis and Their Application in Modern Medicine. *International Journal of Molecular Sciences*, 23(13), 7400. <https://doi.org/10.3390/ijms23137400>
- Genchi, G., Sinicropi, M. S., Lauria, G., Carocci, A., & Catalano, A. (2020). The Effects of Cadmium Toxicity. *International Journal of Environmental Research and Public Health*, 17(11), 3782. <https://doi.org/10.3390/ijerph17113782>
- Gillessen A, &Schmidt HH.(2020). Silymarin as Supportive Treatment in Liver Diseases: A Narrative Review. *Advanced Therapy*. 37(4):1279-1301. doi: 10.1007/s12325-020-0125
- Hano, C., & Abbasi, B. H. (2021). Plant-Based Green Synthesis of Nanoparticles: Production, Characterization and Applications. *Biomolecules*,12(1),31. <https://doi.org/10.3390/biom12010031>
- Hung-Chen Lin, Wei-Ming Hao, Pao-Hsien Chu (2021) Cadmium and cardiovascular disease: An overview of pathophysiology, epidemiology, therapy, and predictive value, *Revista Portuguesa de Cardiologia (English Edition)*, Volume 40, Issue 8, 2021, Pages 611-617, ISSN 2174-2049, <https://doi.org/10.1016/j.repce.2021.07.031>
- Hrabák A, Bajor T, Mészáros G (2008). The inhibitory effect of various indolyl amino acid derivatives on arginase activity in macrophages. *Amino Acids* 34:293–300
- Joardar, S., Dewanjee, S., Bhowmick, S., Dua, T. K., Das, S., Saha, A., & De Feo, V. (2019). Rosmarinic Acid Attenuates Cadmium-Induced Nephrotoxicity via Inhibition of Oxidative Stress, Apoptosis, Inflammation and Fibrosis. *International Journal of Molecular Sciences*, 20(8),2027. <https://doi.org/10.3390/ijms20082027>
- Kazemi, S., Hosseingholian, A., Gohari, S.D., Feirahi, F., Moammeri, F., Mesbahian, G., Z.S. Moghaddam,Z.S., & Ren Q. (2023). Recent advances in green synthesized nanoparticles:from production to application, *Materials Today Sustainability*,Volume 24,100500, <https://doi.org/10.1016/j.mtsust.2023.100500>
- Kaur G., Shivanandappa T.B., Kumar M., &Kushwah A.S.(2020). Fumaric acids protect the cadmium-induced hepatotoxicity in rats: owing to its antioxidant, anti-inflammatory action and aid in recast the liverfunction. *Naunyn-Schmiedeberg's Arch. Pharmacology*. 393:1911–1920
- Khan, F., Shariq, M., Asif, M., Siddiqui, M. A., Malan, P., & Ahmad, F. (2022). Green Nanotechnology: Plant-Mediated Nanoparticle Synthesis and Application. *Nanomaterials (Basel, Switzerland)*,12(4), 673. <https://doi.org/10.3390/nano12040673>
- Lee, K. X., Shameli, K., Yew, Y. P., Teow, S. Y., Jahangirian, H., Rafiee-Moghaddam, R., & Webster, T. J. (2020). Recent developments in the facile bio-synthesis of gold nanoparticles(AuNPs)and their biomedical applications. *International Journal of Nanomedicine*, 275-300.
- Malik, S., Muhammad, K., & Waheed, Y. (2023). Nanotechnology: A Revolution in Modern Industry. *Molecules (Basel, Switzerland)*, 28(2),661. <https://doi.org/10.3390/molecules28020661>.
- Maha M. El-Kady, Iqbal Ansari, Charu Arora, Nidhi Rai, Sanju Soni, Dakeshwar Kumar Verma, Priyanka Singh, Alaa El Din (2023). Mahmoud, *Nanomaterials: A comprehensive review of applications, toxicity, impact, and fate to environment*, *Journal of Molecular Liquids*, Volume57,121046, <https://doi.org/10.1016/j.molliq.2022.121046>
- Mehdi Koushki, Reyhaneh Farrokhi Yekta, Nasrin Amiri-Dashatan (2023). Critical review of therapeutic potential of silymarin in cancer: A bioactive polyphenolic flavonoid, *Journal of Functional Foods*, Volume 104,105502, ISSN 1756-4646, <https://doi.org/10.1016/j.jff.2023.105502>
- Milan, Justyna, Klaudia Niemczyk, and Małgorzata Kus-Liśkiewicz (2022) "Treasure on the Earth—Gold

- Nanoparticles and Their Biomedical Applications" *Materials* 15, no. 9: 335
<https://doi.org/10.3390/ma15093355>
- Momeni, H. R., & Eskandari, N. (2020). Curcumin protects the testis against cadmium-induced histopathological damages and oxidative stress in mice. *Human & Experimental Toxicology*, 39(5), 653–661.
<https://doi.org/10.1177/0960327119895564>
- Miu, Bogdan Andrei, and Anca Dinischiotu. (2022). "New Green Approaches in Nanoparticles Synthesis: An Overview" *Molecules* 27, no. 19: 6472.
<https://doi.org/10.3390/molecules27196472>
- Nabatanzi, A., Nkadimeng, S. M., Lall, N., Kabasa, J. D., & McGaw, L. J. (2020). Antioxidant and Anti-Inflammatory Activities of *Kigelia africana* (Lam.) Benth. *Evidence-based Complementary and Alternative Medicine : eCAM*, 2020, 4352084.
<https://doi.org/10.1155/2020/4352084>
- Nabatanzi A, M Nkadimeng S, Lall N, Kabasa JD, J McGaw L. (2020). Ethnobotany, Phytochemistry and Pharmacological Activity of *Kigelia africana* (Lam.) Benth. (Bignoniaceae). *Plants* (Basel). 2020 Jun 15; 9(6):753. doi: 10.3390/plants9060753
- Niture, S., Lin, M., Qi, Q., Moore, J. T., Levine, K. E., Fernando, R. A., & Kumar, D. (2021). Role of Autophagy in Cadmium-Induced Hepatotoxicity and Liver Diseases. *Journal of Toxicology*, 2021, 9564297.
<https://doi.org/10.1155/2021/9564297>
- Nurakhmetova, Z. A., Azhkeyeva, A. N., Klassen, I. A., & Tatykhanova, G. S. (2020). Synthesis and Stabilization of Gold Nanoparticles Using Water-Soluble Synthetic and Natural Polymers. *Polymers*, 12(11), 2625.
<https://doi.org/10.3390/polym12112625>
- Oueslati, M. H., Ben Tahar, L., & Harrath, A. H. (2020). Synthesis of ultra-small gold nanoparticles by polyphenol extracted from *Salvia officinalis* and efficiency for catalytic reduction of p-nitrophenol and methylene blue. *Green Chemistry Letters and Reviews*, 13(1), 18–26.
<https://doi.org/10.1080/17518253.2019.171120>
- Peana, M., Pelucelli, A., Chasapis, C. T., Perlepes, S. P., Bekiari, V., Medici, S., & Zoroddu, M. A. (2022). Biological Effects of Human Exposure to Environmental Cadmium. *Biomolecules*, 13(1), 36.
<https://doi.org/10.3390/biom13010036>
- Poosa M, Vanapatla SR (2020) Protective effect of Antigonon leptopus (Hook et. Arn) in cadmium induced hepatotoxicity and nephrotoxicity in rats. *Clinical Phytoscience*, 6(1), 32.
- Qu, F., & Zheng, W. (2024). Cadmium Exposure: Mechanisms and Pathways of Toxicity and Implications for Human Health. *Toxics*, 12(6), 388.
<https://doi.org/10.3390/toxics12060388>
- Rafati Rahimzadeh, M., Rafati Rahimzadeh, M., Kazemi, S., & Moghadamnia, A. A. (2017). Cadmium toxicity and treatment: An update. *Caspian Journal of Internal Medicine*, 8(3), 135–145.
<https://doi.org/10.22088/cjim.8.3.135>
- Satarug, S. (2024). Is chronic kidney disease due to cadmium exposure inevitable and can it be reversed?. *Biomedicines*, 12(4), 718.
- Takemura, K.; Board, P.G.; Koga, F. A (2021). Systematic Review of Serum γ -Glutamyltransferase as a Prognostic Biomarker in Patients with Genitourinary Cancer. *Antioxidants* 10, 549.
<https://doi.org/10.3390/antiox10040549>
- Teschke R. (2022). Aluminum, Arsenic, Beryllium, Cadmium, Chromium, Cobalt, Copper, Iron, Lead, Mercury, Molybdenum, Nickel, Platinum, Thallium, Titanium, Vanadium, and Zinc: Molecular Aspects in Experimental Liver Injury. *International Journal of Molecular Sciences*, 23(20), 12213.
<https://doi.org/10.3390/ijms232012213>
- Tinkov, A. A., Filippini, T., Ajsuvakova, O. P., Skalnaya, M. G., Aaseth, J., Bjørklund, G., & Skalny, A. V. (2018). Cadmium and atherosclerosis: A review of toxicological mechanisms and a meta-analysis of epidemiologic studies. *Environmental Research*, 162, 240–260.
- Uhuo, E. N, Ezeanyika, L.U.S & Ogugua, V.N (2019). Oxidative and biochemical parameters analysis of alloxan-induced diabetic rats administered methanol leaf and fruit extracts of *Kigelia africana*. *London Journal of Research in Science: Natural and Formal*.
- Uhuo, E. N., Obike, C. A., Joshua, P. E., Alaebo, P. O., & Anyanwu, R. C. (2025). Mitigation of cadmium-induced hepatotoxicity by orally administered *Xylopia aethiopica* synthesized silver nanoparticles in rats. *Journal of Molecular Histology*, 56(3), 187.
- Uhuo, E. N., Nwuke, C. P., Oriaku, C. E., & Chilaka, J. O. (2021). Biochemical and hormonal studies of metoclopramide-induced hyperprolactinemic female rats administered ethanol Leaf Extract of *Kigelia africana*. *Comparative Clinical Pathology*, 30(3), 371–377. <https://doi.org/10.1007/s00580-021-03224-1>
- Varghese, R., Almalki, M. A., Ilavenil, S., Rebecca, J., & Choi, K. C. (2019). Silver nanoparticles synthesized using the seed extract of *Trigonella foenum-graecum* L. and their antimicrobial mechanism and anticancer properties. *Saudi Journal of Biological Sciences*, 26(1), 148–154.
<https://doi.org/10.1016/j.sjbs.2017.07.001>
- Varshney, R., & Kale, R. K. (1990). Effects of calmodulin antagonists on radiation-induced lipid peroxidation in microsomes. *International Journal of Radiation Biology*, 58(5), 733–743.
- Xin, JS; Guo, JC; Zhu, HQ; Song, XX (1991). An assay for superoxide dismutase in mammalian tissue homogenates. *Analytical biochemistry*, 179(1), 8–18.
- Xing, M., Gao, M., Li, J., Han, P., Mei, L., & Zhao, L. (2022). Characteristics of peripheral blood Gamma-glutamyl transferase in different liver diseases. *Medicine*, 101(1), e28443. <https://doi.org/10.1097>

- Yang, Y., Hassan, M. F., Ali, W., Zou, H., Liu, Z., & Ma, Y. (2025). Effects of cadmium pollution on human health: A narrative review. *Atmosphere*, 16(2), 225.
- Yaqoob, A. A., Ahmad, H., Parveen, T., Ahmad, A., Oves, M., Ismail, I. M. I., Qari, H. A., Umar, K., & Mohamad Ibrahim, M. N. (2020). Recent Advances in Metal Decorated Nanomaterials and Their Various Biological Applications: A Review. *Frontiers in chemistry*, 8, 341. <https://doi.org/10.3389/fchem.2020.00341>
- Zuhrotun, A., Oktaviani, D. J., & Hasanah, A. N. (2023). Biosynthesis of Gold and Silver Nanoparticles Using Phytochemical Compounds. *Molecules (Basel, Switzerland)*, 28(7), 3240. <https://doi.org/10.3390/molecules28073240>

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher. The publisher remains neutral with regard to jurisdictional claims.

Submit your next manuscript to NJBMB at
<https://www.nsbmb.org.ng/journals>