

***Cocos nucifera* Water Ameliorated Hepatic Complications and Attenuated Oxidative Stress in Cadmium-Induced Hepatotoxicity**



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ABSTRACT

Objectives: The effect of *Cocos nucifera* water on indices of liver function and oxidative stress in cadmium-induced hepatotoxicity was investigated in albino rats.

Methods: The study utilized 30 Wistar rats divided into 6 groups (A-F) (n=5). Groups A and B served as controls and were given normal saline only via oral probe. Hepatotoxicity was induced in groups B, D, E, and F by oral administration of 15 mg cadmium/kg body weight for 14 consecutive days. Group B remained untreated; Groups D through F were treated with varying doses of *Cocos nucifera* water (1.0-3.0) mL/kg b.wt for 14 days and group C received 2.0 mL of *Cocos nucifera* water without induction. Earlier, the proximate, vitamin, and mineral contents of *Cocos nucifera* water were determined using standard methods.

Results: The results showed proximate compositions in the following order: moisture > carbohydrates > ash > fat > protein, mineral compositions were as follows: potassium > magnesium >

calcium > iron, and vitamins as follows: vitamin C > B9 > E > B1. Administration of cadmium to rats caused a significant ($p < 0.05$) increase in the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), malondialdehyde (MDA) concentration and decreased catalase (CAT), superoxide dismutase (SOD) and reduced glutathione (GSH). Treatment with *Cocos nucifera* water significantly ($p < 0.05$) decreased the effects of cadmium in rats. Histopathological examination also indicated that the water moderately restored the liver architecture close to normal.

Conclusion: The results of this study suggest that *Cocos nucifera* water maybe beneficial in treating liver complications.

Keywords: Cadmium; *Cocos nucifera* Water; Hepatotoxicity; Oxidative Stress; Medicinal plants

Introduction

Plant resources have remained an integral part of human society throughout history. After having met the primary needs such as food and shelter, men searched for a suitable remedy among the plants to cure various diseases. *Cocos nucifera* palms are unbranched, monoecious trees with a smooth, columnar, light gray-brown trunk, usually 9-18 m high and sometimes higher (up to 30 m); there are also dwarf selections. The fruit consists of (from the outside in) a thin hard shell (exocarp), a thicker layer of fibrous mesocarp (shell), the hard endocarp (shell), the white endosperm (kernel), and a large cavity filled with aqueous fluid (Coconut water or milk). The endosperm is soft and gelatinous when immature but becomes firm with maturity. *Cocos nucifera* water or milk is abundant in unripe fruit but is gradually absorbed as it ripens. The fruits are initially green and become brownish as they ripen; yellow varieties go from yellow to brown. (Khan, 2003). *Cocos nucifera* water consists of 95.5% water, 4%

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sugar, 0.1% fat, 0.02% calcium, 0.01% phosphorus, 0.5% iron, considerable amounts of amino acids, mineral salts, vitamin B complex, Vitamin C and cytokines, etc. Other components in Cocos nucifera water are sugar (glucose), sugar alcohols, lipids, amino acids, nitrogen compounds, organic acids, and enzymes. The characteristic aroma of Cocos nucifera is contributed by delta lactones. The nutritional composition of Cocos nucifera water is, however, influenced by several factors, including the state of maturity, soil, and environmental conditions.

Cadmium (Cd), a toxic and nonessential element, is widely used in electroplating, pigments, paints, welding, and batteries, resulting in biotic and abiotic environments. In contrast to organic compounds, Cd is not biodegradable and has a very long biological half-life. It has been found that Cd causes a wide range of biochemical and physiological dysfunctions in humans, laboratory animals, and plants. Many mammalian organs are affected by Cd, including the kidney, liver, testes, lungs, pancreas, prostate, ovaries, and placenta. reported an adverse effect of Cd on spermatogenesis through the generation of free radicals. Growing evidence has also shown that Cd alters antioxidant defense systems and increases the production of cellular reactive oxygen species (ROS) such as singlet oxygen, hydrogen peroxide, and hydroxyl radicals. By reacting with macromolecules, ROS can lead to oxidative stress within cells and cause damage such as mutations in DNA, destruction of protein function and structure, peroxidation of lipids as well as changes in gene expression and apoptosis. Tissue levels of malondialdehyde (MDA) and the activities of superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) are proven indicators of oxidative stress. investigated the role of Cd in changing antioxidative defense systems and in inducing apoptosis in the hepato-pancreas of *S. henanense*. suggested that Cd-induced apoptosis could be linked to oxidative stress. Several reports have shown that oxidative stress is an important mechanism of Cd toxicity.

Cocos nucifera water has several culinary uses. It is renowned in Traditional Chinese Medicine for bolstering the heart and boosting endurance and its oils are used as insect repellants in Chinese culture. Many studies have shown that the antiviral, antibacterial, anti-inflammatory, and antioxidant properties of Cocos nucifera water can help alleviate a range of mild or severe health conditions. This nutrient-rich drink has been used to help regulate blood pressure, blood sugar, and cholesterol levels, and it has been found to increase energy levels and increase metabolism in the human body. It has also been implicated in the treatment of stomach flu, dysentery, indigestion, constipation, intestinal worms, urethral stones, kidney dysfunction, dry and itchy skin, age spots, and wrinkles. Cocos nucifera water can help raise high-density (good) lipoprotein cholesterol, making it a wonderful natural treatment for maintaining good cardiovascular health. Young Cocos nucifera water has estrogen-like properties. It mixes easily with blood and was used in emergency transfusions during World War II. Cocos nucifera water can also serve as a short-term intravenous fluid supply. This is possible because it contains high levels of sugar and other salts that allow it to be used in the bloodstream, similar to the modern lactate Ringer's solution or a dextrose water solution as an intravenous solution. In Eastern Nigeria, Cocos nucifera water is used for various medicinal purposes, including the treatment and management of various conditions such as gastrointestinal disorders, high blood pressure, dehydration, kidney dysfunction, anxiety, etc. Hence, the motivation behind this study on Cocos nucifera water in cadmium induced hepatotoxic rats

Methods

Chemicals and Reagents

Chemicals used in this study were of high analytical grade and were bought from Sigma Aldrich (St. Louis, Mo, USA) and the reagents used for some assays were commercial kits and products of Randox Laboratories Ltd, UK.

Collection of nuts

In Mgbabor in Abakaliki, Ebonyi state, Nigeria, a total of 30 Cocos nucifera nuts (all same type, Green high) were collected. The Cocos nucifera nuts were identified and authenticated by a taxonomist from the Department of Applied Biology at Ebonyi State University, Abakaliki. The Cocos nucifera water was carefully collected by draining it through drilled holes in the macrophytes, and the water was collected in the beaker and used immediately. The water was carefully harvested and checked to ensure that there were no peel residues in it and given fresh (George, 2008)

Proximate, Mineral and vitamin Analysis of Cocos nucifera, Water

Percentage compositions of protein, ash, moisture, and carbohydrates were determined using the method of the Association of Official Analytical Chemists A.O.A.C (1995), while the fat content was determined by the gravimetric solvent extraction method described by (James, 1995). Moreover, mineral composition, potassium, calcium, magnesium, and iron were performed by the method of (Moyo et al., 2018) while the vitamins were determined according to the methods of A.O.A.C. (1995)

Experimental animals and design

Experimental Animals

A total of thirty albino rats (100-190 g) were obtained from Animal House, University of Nigeria, Nsukka, Enugu State. They were housed under standard laboratory conditions for two weeks for acclimatization and fed rodent chow and water ad libitum in the Animal House of the Biochemistry Department at Ebonyi State University in Abakaliki. The animals were divided into 6 groups (n = 5). Group A served as a normal control given ad libitum with rat chow and water. Toxicity was induced in groups B, D, E, and F by oral administration of 15 mg / kg body weight cadmium for 14 consecutive days. Group B, which served as a positive control, was left without treatment. Group C received 2.0 ml / kg of Cocos nucifera water via oral gavage without induction. Groups D, E, and F were treated with 1.0, 2.0, and 3.0 ml/kg of Cocos nucifera water, respectively following an earlier report by (Agbafor, 2015) with minor modifications. The cadmium exposure (14 days) and treatment with Cocos nucifera water (once per day) lasted for 28 days (4 weeks). The weight of the rats was measured and recorded before and after the experimental treatments. Animals were sacrificed and blood samples were drawn from the animals after an overnight fast by cardiac puncture under light anesthesia using diethyl ether.

Determination of Liver Function Parameters

The activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were assayed according to the method of (Reitman, 1957), while alkaline phosphatase (ALP) activity was assayed by colorimetric method as described by (Klein, 1960).

Determination of Oxidative Stress Parameters

Determination of malondialdehyde (MDA) level

MDA was determined by spectrophotometric method as described by (Wallin, 1993). In a nutshell, the test tube was filled with exactly 0.1 ml of sample, 0.9 ml of distilled water, 0.5 ml of TCA reagent, and 0.5 ml of TBA reagent before being sealed. The test tube was incubated for 40 minutes at 95 degrees Celsius. After that, the test tube was allowed to cool in the water for a few minutes before a precise 0.1 ml of SDS (sodium dodecyl sulfate) solution was added to it. The absorbance of the sample was measured at 532 and 600 nm in comparison to the blank reagent.

$$\text{Calculation: \% TBARS} = \frac{A_{532} - A_{600}}{0.5208 \times 0.1} \times \frac{100}{1}$$

Determination of catalase (CAT) activity

CAT activity was assayed according to the method described by . In brief, 2.5 mL of phosphate buffer and 2 mL of H₂O₂ were added to the test tube exactly at the same time. Following that, 0.5 mL of the sample was also put into the test tube. Two milliliters of dichromate acetic acid reagent were added to a one-milliliter aliquot of the reaction mixture. The absorbance was measured at 240 nm against a blank at a rate of one reading per minute.

$$\text{Catalase concentration (U/L)} = \Delta A / \text{min} \times V_T / \Sigma \times V_s,$$

Where:

ΔA = change in absorbance, V_T = total volume, V_s = sample volume and Σ = molar extinction

Determination of the SOD activity

The method described by was used to determine the activity of SOD. Based on the inhibition of nitroblue tetrazolium (NBT) reduction. The sample was mixed with 2.95 ml of 0.05 M sodium carbonate buffer (pH 10.2) and 0.03 ml of epinephrine in 0.005 M HCl to begin the reaction, which took 0.02 ml in total. Similarly, the blank had 2.95 ml buffer, 0.03 ml of epinephrine, and 0.02 ml of distilled water. SOD activity was determined by measuring the change in absorbance at 480 nm for 5 minutes with a spectrophotometer. $\Sigma = 4020 \text{ M}^{-1} \text{ cm}^{-1}$.

$$\text{Calculation: } \Delta A / \text{min} \times V_T / \Sigma \times V_s,$$

Where:

ΔA = change in absorbance, V_T = total volume, V_s = sample volume, and Σ = molar extinction

Determination of reduced GSH

This was determined using the method of . Reduced GSH constitutes the vast majority of nonprotein sulfhydryl groups in this assay. The procedure was straightforward: 0.2 ml of serum was combined with 2 ml of 10% trichloroacetic acid and centrifuged to separate the protein. Then 2mL of phosphate buffer (pH 8.4), 0.5mL of 5, 5-dithio, bis (2-nitrobenzoic acid), and 0.4ml of double distilled water to 0.01ml of the supernatant to achieve the desired pH. The absorbance was read at 412 nm after the mixture had been vortexed. The concentration of GSH was calculated as follows:

$$\text{Plasma GSH concentration} = \frac{A_{\text{sample}} - A_{\text{blank}}}{A_{\text{standard}} - A_{\text{blank}}} \times \text{Standard (mol/L)}$$

Histological examination of hepatic tissue

For brevity, in this investigation, liver tissue was fixed in 10% formal saline for three days in a container with light-tight lids to prevent autolysis, increase staining quality, and help the optical

differentiation of cells. The tissue was dried to remove water that was not miscible with xylene and wax using different grades of alcohol ranging from 50 percent to absolute alcohol for 30 minutes on each side for a total of three hours. After the dehydrated tissue had been cleaned, it was immersed in three changes of xylene for 30 minutes each to remove the alcohol that had accumulated on it. A hot oven temperature of 550C was used to impregnate and penetrate the cleared tissue to remove the clearing agent (xylene). The tissue was passed through three changes of molten paraffin wax in a hot air oven for 30 minutes to remove the clearing agent. It was necessary to bury or embed the infiltrating tissue in molten paraffin wax in an embedded mold before the wax could be solidified. It was necessary to adhere a paraffin block of tissue to a wooding block using a hot spatula that was sandwiched between the wooding block and the paraffin wax. It is necessary to remove the spatula for the wax to be melted and solidified. To stain the tissue, it was sectioned using a rotary microtome and trimmed to 15 microns to acquire the cutting surface of the tissue. The tissue was then sectioned at 5 microns and dried in a hot plate before staining was completed. The segment was hydrated and then cleared with xylene to complete the process. After that, it was immersed in hematoxylin. After being cleaned with tap water, the portion was immersed in an acid-alcohol solution for 15 minutes. The piece was soaked in eosin stain for 15 minutes, after which the excess stain was washed away with tap water. The section was dehydrated with ethanol and mounted on a microscope slide using a resinous medium containing emission oil, after which the cells were examined.

Statistical Analysis

The data obtained were expressed as mean $\pm$ STD and subjected to one-way analysis of variance (ANOVA) followed by Duncan multiple range comparison and Prism graph pad 7. Values $p < 0.05$ were considered significant

Results

Chemical Composition of Cocos nucifera water

The results of the proximate composition of Cocos nucifera water showed the following order of occurrence: moisture > carbohydrates > ash > fat > protein (Figure 1). Potassium content was observed to have the highest value followed by magnesium, calcium and the least iron in mineral composition (Figure 2). The vitamin content of Cocos nucifera water revealed the following order of occurrence vitamin C > B₉ > E > B₁, while vitamin A was completely absent (Figure 3).

Effect of Cocos nucifera Water on Liver Enzymes of Cd-induced Hepato-toxicity in Albino Rats.

The results on liver function enzymes in Cd-induced hepatotoxicity rats showed a significant ($p < 0.05$) increase in ALP, AST, and ALT levels in the groups that received 15mg/kg (b.w) of Cd only relative to other groups as shown in Figure 4, 5 and 6. However, the administration of rats with different doses of Cocos nucifera water caused a reversal of the trend significantly ($p < 0.05$) reducing the activity of the liver enzyme parameters to levels similar to the normal control (Figures 4, 5, and 6).

Effect of Cocosnucifera Water on Oxidative Stress Indices in Cd-induced Hepato-toxicity in Albino Rats.

The results on oxidative stress index in Cd-induced hepatotoxicity in albino rats showed a significant ($p < 0.05$) decrease in the levels of SOD, Catalase, and GSH indices as shown in Figures 8 and 9, and 10 and a significant ($p < 0.05$) increase was observed in MDA level (Figures 7) on the administration of 15mg/kg (b.w.) of Cd. However, treatment of the rats with different doses of Cocos nucifera water caused a reversal of the trend significantly ($p < 0.05$) reducing the activity of the oxidative parameters to levels like the normal control. However, the effect was not dose-dependent for SOD activity.

Effect of Cocos nucifera Water on Histopathology of Liver in Cd-induced Hepato-toxicity in Albino Rats.

The results on histopathological effect on the liver showed a severe aggregate of inflammatory cells (AIC) around the hemorrhagic area, indicating severe chronic hepatitis features as shown in Plate 2 on the administration of 15 mg/kg b.w. of Cd. However, treatment of cadmium-intoxicated albino rats with different doses of Cocos nucifera water caused a moderately healing effect with mild aggregates of intralobular inflammation (AILI) around the intrahepatic hemorrhage (IHH) in r1 and mild congestion of the portal vein (CPV) as shown in Plates 4, 5 and 6. However, the liver cells showed well-perfused normal lobular architecture with central vein (CV), portal triad (PT), and hepatocytes (H) with a mild aggregate of inflammatory cells (AIC) within the portal triad otherwise normal as shown in Plates 1 and 4 in Figure 11.

Discussion

This study investigated the impact of Cocos nucifera water on cadmium-induced hepatotoxicity. The proximate, mineral, and vitamin contents of C. nucifera water were quite fascinating. Moisture, carbs, ash, fat, and protein were all detected in considerable amounts. This was in agreement with an earlier report by showing that C.nuciferawater contains crude protein, crude fat, moisture, ash, and carbohydrates. Nonetheless, the current study found some changes in the amounts of various proximate components, which could be due to differences in soil factors at different geographical sites where plants were obtained for proximate research.

Even though lipids and proteins were also present in substantial proportions, our findings demonstrated that C.nucifera water is a better source of carbohydrates than the three basic macromolecules investigated (carbohydrates, lipids, and protein). The high quantities of lipids and carbohydrates in C.nucifera water may explain its widespread use in nutrition around the world, as well as its utility as a source of energy for a variety of biological processes. Because of the high protein content of C.nucifera water, it may have important immunological, physiological, nutritional, and pharmacological impacts on the body, contributing to general health and well-being. The relatively high composition of protein, carbohydrates, and fats present in C. nuciferawater indicates that the plant could be beneficial in both human and livestock nutrition.

Mineral content indicated potassium to have the highest value followed by magnesium, calcium, and iron. The finding of this study is similar to the work of, who reported the amount of potassium, magnesium, and sodium to be higher than other minerals evaluated in C.nuciferawater. This work also relates closely to the report of who estimated the nutritive potentials of C.nucifera water as magnesium, calcium, potassium, and iron were all present. However, the mineral contents of C.nuciferawater in this study were higher than the values

reported by, who determined the mineral composition of C. nucifera water in coastal areas of Pakistan, as follows: potassium, magnesium, calcium, and iron. Minerals are important as a constituent of bones and teeth, as well as in the regulation of nerve and muscle function, as enzyme cofactors (e.g., kinases), as constituents of intracellular fluid, and as regulators of acid-base balance, osmotic pressure, nerve impulse conduction, and the Na⁺/K⁺ ATPase system. Minerals are also important as a constituent of bones and teeth, as well as in the regulation of nerve and muscle function, as enzyme While iron is a significant component of erythrocyte pigment, hemoglobin is an even more vital component'.

The vitamin content of C.nucifera water revealed the following order of occurrence vitamin C > B9 > E > B1, while vitamin A was completely absent. This study correlates with the report of who asserted that the nutritive potential of C.nucifera water contains the following: vitamin C, vitamin B1, and vitamin B9. The result of this study is not fully in agreement with the report of, who conducted the study on the antioxidant activity of C.nucifera water, and reported that vitamin C and vitamin E were the two major vitamins present in C.nuciferawater. However, this finding is more in agreement with the work of which reported that this value for vitamin E was also present in C.nucifera water. Vitamins are micronutrients that play a vital role in a healthy living. The body needs them in relatively small amounts, in comparison with other nutrients.

Albino rats were used in an in vivo biochemical investigation to determine the effects of C.nucifera water on several indices of liver function and oxidative stress after being exposed to cadmium-induced hepatotoxicity. Figures 4, 5, and 6 show that the levels of alkaline phosphatase (ALP), aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were significantly higher in the groups that received only 15mg/kg (b.w.) of Cd, compared to the other groups, indicating that Cd-induced hepatotoxicity rats had a significant ($p < 0.05$) increase in liver function enzymes. The administration of varied dosages of C.nucifera water to the rats, on the other hand, resulted in a statistically significant ($P > 0.05$) reversal of the trend, with the activity of the liver enzyme parameters returning to values comparable to those of the normal control. The results of this investigation revealed that cadmium administration resulted in a statistically significant increase ($p < 0.05$) in the activity of the enzymes ALP, AST, and ALT when compared to the normal control rats. CdCl₂ treatment for 14-21 days in rats at a dose of 15 mg/kg body weight induced an increase (liver damage) in the levels of ALT, AST, and ALP that was statistically significant ($p < 0.05$) different from the control group, according to Joseph and colleagues. The increase in serum hepatic enzymes has been related to damage to the structural integrity of the liver because these enzymes are ordinarily contained within the cytoplasm of hepatocytes and are only released into circulation when there is a breakdown in the cellular structure of the liver. It was discovered that treating albino rats with C.nucifera water resulted in a statistically significant ($p < 0.05$) reverse of the effects of cadmium intoxication, as evidenced by the statistically significant ($p < 0.05$) lowering of liver enzymes in the treated groups. According to the findings of this study, heavy metals such as cadmium administration in rats can cause an increase in the activities of ALT, ALP, and AST. However, the restorative effect of C.nucifera water may be attributed to the presence of antioxidant properties in C.nucifera water, which exert a membrane-stabilizing effect that prevents damage to hepatocytes.

During a subsequent investigation, it was discovered that the

treatment of albino rats with cadmium (15mg/kg body weight) resulted in hepatotoxicity, as demonstrated by a statistically significant ($p < 0.05$) decrease in CAT and SOD and an elevated ($p < 0.05$) MDA level when compared to the normal control group. In this work, Cocos nucifera water was shown to be helpful in reversing the effects of cadmium-induced hepatitis in albino rats on oxidative stress indicators in a dose-dependent way, primarily through the reduction of oxidative stress levels. According to the findings of, polyphenols isolated from virgin Cocos nucifera water have a protective effect against sub-chronic cadmium hepatotoxicity in rats, and Cd has a significant negative effect on the antioxidant defense system, with SOD, CAT, and GSH content in the liver being significantly decreased. The presence of MDA in the liver indicated a significant increase in hepatic lipid peroxidation. reported on the hepatoprotective and antioxidant effect of tender Cocos nucifera water against carbon tetrachloride-induced liver injury in rats; that increased lipid peroxidation was evidenced by elevated levels of a thiobarbituric acid reactive substance (TBARS) viz, MDA, and by a significant decrease in antioxidant enzymes activities, such as SOD, CAT, GPx and glutathione reductase (GR) and reduced GSH content in the liver. This present study also agreed with a study looked into the effect of tender Cocos nucifera water on antioxidant enzymes like SOD, CAT, GPx, and lipid peroxidation (MDA) in mercury-exposed workers, and found the mean levels of SOD, CAT, and GPx in the treatment group were higher than those in the control group, while MDA was lower in the treatment group. Histopathological examination reveals that the liver of normal control albino rats has a normal histological appearance (x400) (H/E) and shows well-perfused normal lobular architecture with the central vein (CV), portal triad (PT),

and hepatocyte (H) (Figure 11; Plate 1), whereas administration of 15mg/kg b. w. of Cd to the albino rats (x400) reveals chronic hepato-cellular degeneration with a focal area of intrahepatic hemorrhage (IHH). The overall features may be because of consistency with chronic hepatitis (Figure 11; Plate 2). The result correlates with who reported that several morphological changes in hepatic tissue were noted after intoxication with Cd. These results agreed with that of who revealed severe hepatic necrosis, fatty changes, degeneration signs, and inflammatory cell infiltration of Cd administrated rats. It is possible that the production of extremely reactive radicals and subsequent lipid peroxidation in the liver of animals treated with Cd is responsible for the histological alterations observed. Histopathological changes in the liver of albino rats (400) after injection of 2.0 ml/kg body weight of untreated Cocos nucifera water demonstrate well-perfused hepatic tissue with modest aggregation of inflammatory cells (AIC) within the portal tract, but the liver is otherwise normal (Figure 11; Plate 3). Treatment of albino rats induced with 15 mg/kg body weight of Cd and treated with 1.0, 2.0, and 3.0 ml/kg body weight of Cocos nucifera water of histological analysis of the liver in each group are shown in (Figure 11; Plates 4, 5 and 6) were observed with less incidence of dilated sinusoids and binuclear liver cells (BN), indicating recovery of liver cell from the damage caused by cadmium. Nevertheless, treatment of albino Plate 6 showed moderate healing with mild accumulation of intralobular inflammation (AILI) around the intra-hepatic hemorrhage (IHH) and slight congestion of the portal vein (CPV), indicating that a higher dose of Cocos nucifera water (3.0 ml/kg) can promote more rapid and better recovery. This recovery must have occurred because of the presence of antioxidant activity in Cocos nucifera water, which was present at the time.

List of Figures

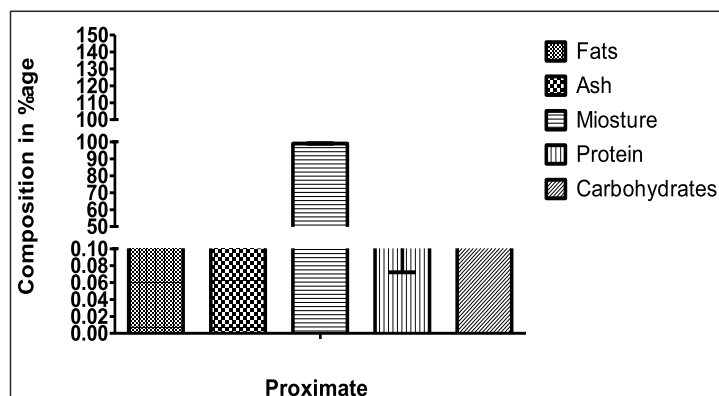


Figure 1: Proximate Composition of Cocos nucifera Water. Data are shown as mean $\pm$ S.D (n=3).

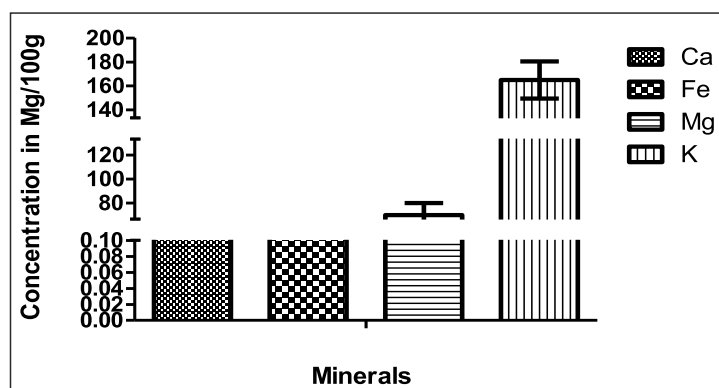


Figure 2: Mineral Composition of Cocos nucifera Water. Data are shown as mean $\pm$ S.D (n=3).

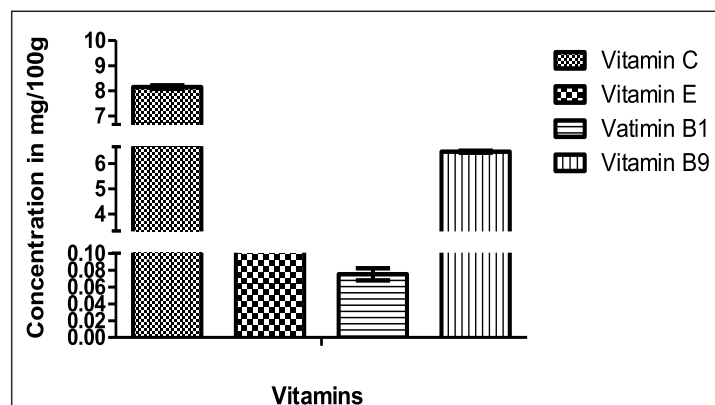


Figure 3: Vitamins Composition of Cocos nucifera Water. Data are shown as mean $\pm$ S.D (n=3).

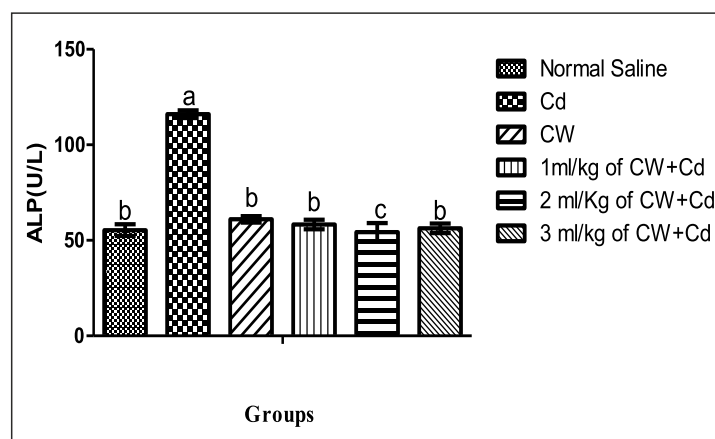


Figure 4: Effect of *Cocos nucifera* Water on alkaline phosphatase activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant differences at $P < 0.05$. Cd= Cadmium CW= *Cocos nucifera* Water

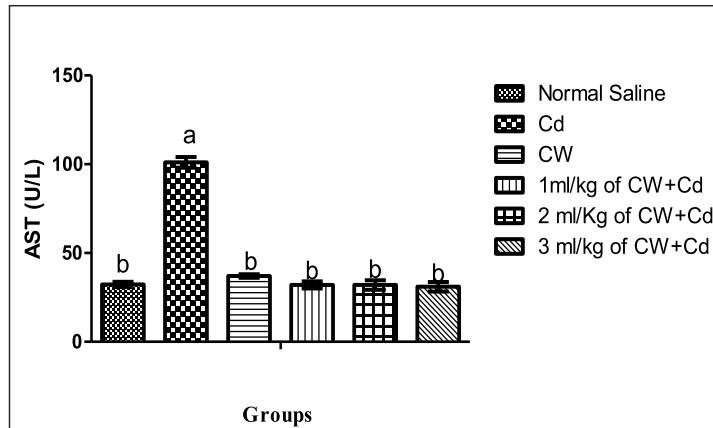


Figure 5: Effect of *Cocos nucifera* Water on aspartate aminotransferase activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant differences at $p < 0.05$. Cd= Cadmium CW= *Cocos nucifera* Water

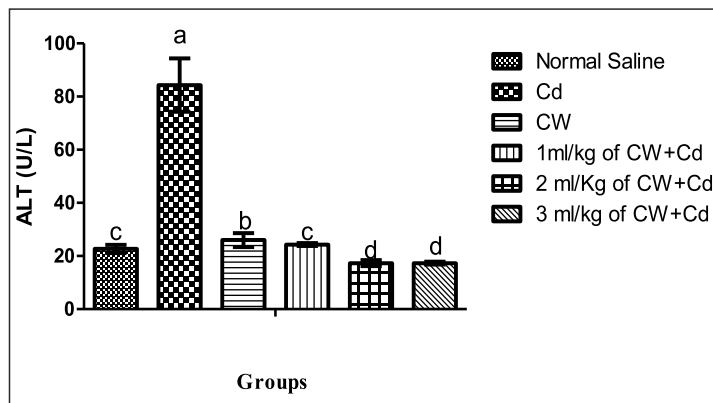


Figure 6: Effect of *Cocos nucifera* water on alanine amino transferase activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant difference at $p < 0.05$

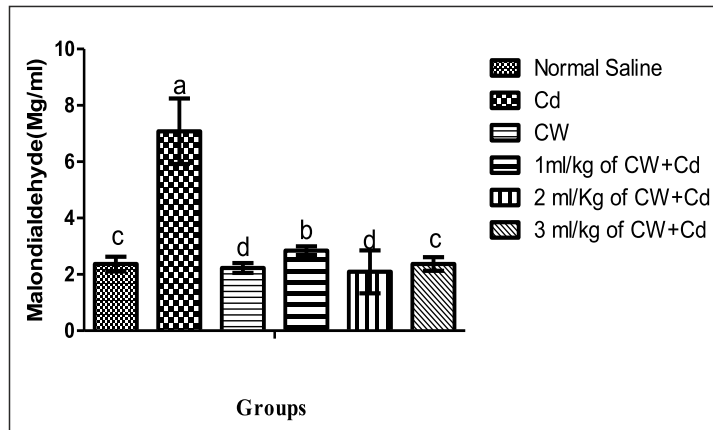


Figure 7: Effect of *Cocos nucifera* water on malondialdehyde activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant differences at $p < 0.05$.

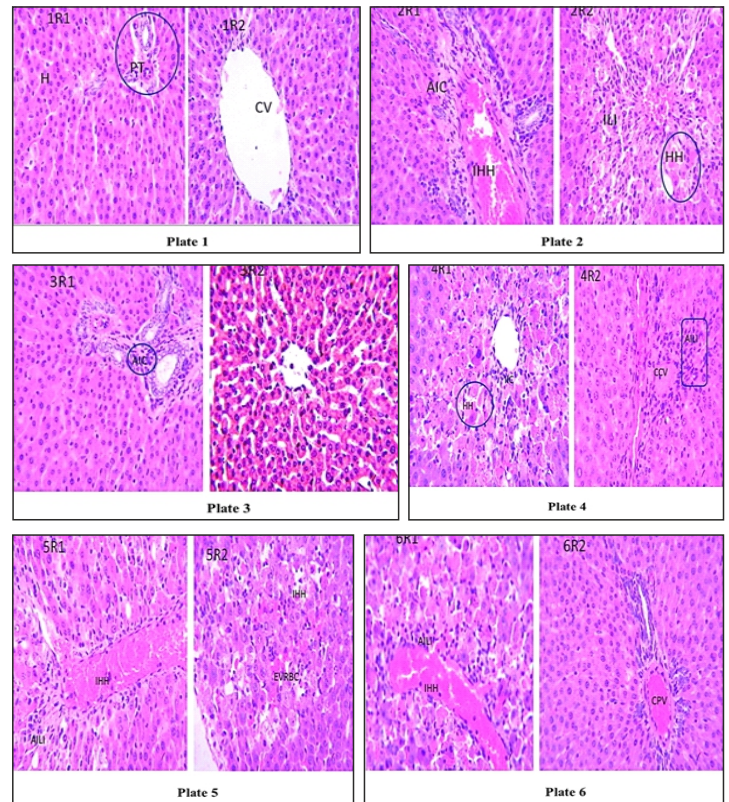


Figure 11: Plate 1: Photomicrograph of normal liver section (1r1r2) (x400) (H/E) showing well perfused normal lobular architecture with central vein (CV), portal tract (PT) and hepatocyte (H);

Plate 2: Photomicrograph of liver section of rats (2r1r2) administered with 15 mg/kg b. w. of cadmium only (x400) (H/E) showing chronic hepatocellular degeneration with focal area of intra hepatic hemorrhage (IHH), severe aggregate of inflammatory cell (AIC) around the hemorrhagic area, severe intra lobular inflammation (ILI) in r2 with hypertrophied hepatocyte (HH) on the background. The overall features are consistent with chronic hepatitis; Plate 3: Photomicrograph of liver section of rats (3r1r2) administered with 2.0 ml/kg b. w. of *Cocos nucifera* water only (x400) (H/E) showing well perfused hepatic tissue with mild aggregate of inflammatory cell (AIC) within the portal tract otherwise normal; Plate 4: Photomicrograph of liver section of rats (4r1r2) administered with 15mg/kg of Cd and 1.0ml/kg b. w. of *Cocos nucifera* water (x400) (H/E), showing mild healing with moderate infiltration of inflammatory cell (IIC) and hypertrophied hepatocyte (HH) around the central vein in 4r1 and moderate aggregate of intralobular inflammation (AILI) around the congested central vein (CCV) in r2; Plate 5: Photomicrograph of liver section of rats (5r1r2) administered with 15mg/kg of Cd and 2.0ml/kg b. w. of *Cocos nucifera* water (x400) (H/E), showing mild to moderate healing with moderate aggregate of intralobular inflammation (AILI) around the intra hepatic hemorrhage (IHH) in 5r1 and mild vacuolation with extravasation of red blood cell (EVRBC) on the background; Plate 6: Photomicrograph of liver section of rats (6r1r2) administered with 15mg/kg of Cd and 3.0 ml/kg b. w. of *Cocos nucifera* water (x400) (H/E), showing moderate healing with mild aggregate of intralobular inflammation (AILI) around the intra hepatic hemorrhage (IHH) in 6r1 and mild congestion of the portal vein (CPV).

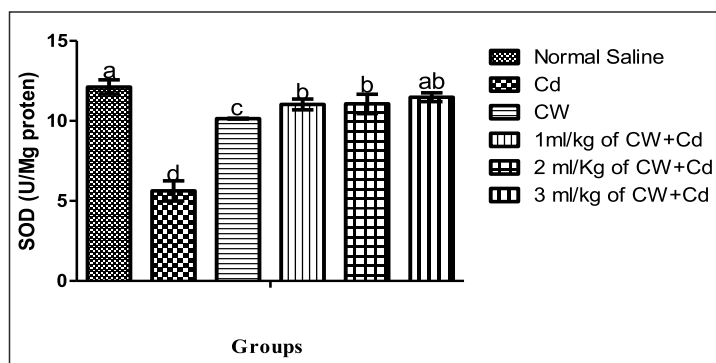


Figure 8: Effect of *Cocos nucifera* water on SOD activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant differences at $p < 0.05$. Cd=Cadmium. CW=Cocos nucifera Water

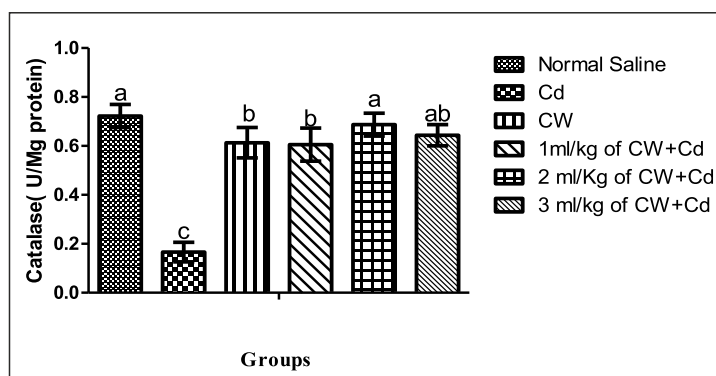


Figure 9: Effect of *Cocos nucifera* water on catalase activity in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant difference at $p < 0.05$. Cd=Cadmium CW=Cocos nuciferawater

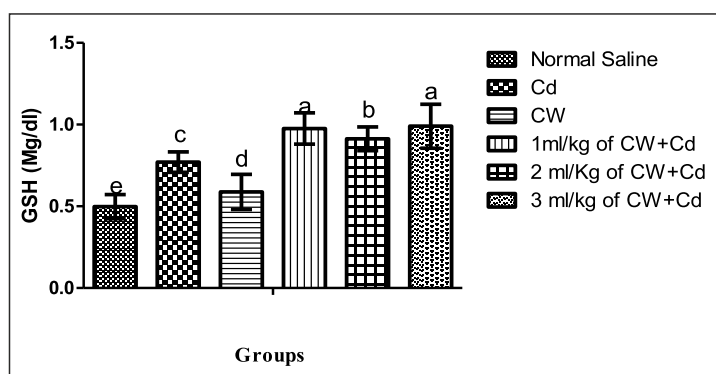


Figure 10: Effect of *Cocos nucifera* water on reduced glutathione level in Cd-induced Hepato-toxicity in rats. Data are shown as mean $\pm$ S. D (n=5). Mean values with different alphabets showed significant differences at $p < 0.05$. Cd=Cadmium CW=Cocos nuciferawater

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