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Original Research Article

Assessment of the Effect of Cashew (*Anacardium occidentale L.*) Nut-Supplemented Diet on Key Biochemical Indices Relevant to Cardiac Function in Cisplatin-Induced Cardiotoxic Rats

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ABSTRACT

Cardiotoxicity can develop as a result of exposure to certain chemicals, poisons, or infectious agents as well as the continued use of higher doses of some medications. Natural plant foods such as cashew nut (*Anacardium occidentale* L.) may have free radical scavenging activity, thereby may play an important role in protecting the heart from chemotherapy-related cardiac dysfunction. In this study, the effect of cashew nut-supplemented diet on key indices relevant to cardiac function in cisplatin-induced cardiotoxic rats was evaluated. The rats were divided into six groups (n=6): rats fed a basal diet; cisplatin-induced rats fed a basal diet; cisplatin-induced rats fed a diet supplemented with processed cashew nut (10 and 20%); healthy rats fed a diet supplemented with processed cashew nut (10 and 20%) for fourteen days. Cisplatin-treated rats showed increased activities of acetylcholinesterase and butyrylcholinesterase, adenosine deaminase, monoamine oxidase, phosphodiesterase-5 and arginase activities with a concomitant decrease in levels of nitric oxide, total thiol, total antioxidant capacity and reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase and glutathione-S-transferase activities both in the heart and plasma when compared with control. However, dietary supplementation with cashew nut significantly attenuated the cisplatin-evoked disturbances in the above-mentioned parameters. Also, feeding of experimental rats with cashew nut-supplemented diet for fourteen days restores significantly the heart histological alteration caused by cisplatin. Taken together, these findings imply that eating cashew nuts may represent a novel cardioprotective strategy during chemotherapy based on cisplatin. Therefore, it could be used as functional diet to prevent cardiac dysfunction caused by cisplatin.

Keywords: Cashew nut; cisplatin; cardiac dysfunction; heart; oxidative stress; histology.

Introduction

Cardiotoxicity is defined as myocardial injury and electrophysiological malfunction of the heart.[1] According to Berardi *et al*.,[2] it may be brought on by chemotherapy treatments using cytotoxic medicines such as doxorubicin, epirubicin, cisplatin, and certain cardiotoxins. Cisplatin is a potent anticancer drug that has shown promise in treating various cancers, including testicular, ovarian, cervical, bladder, and lung cancers as well as solid tumors refractory to prior treatment plans.[3] Regretfully, prior studies have demonstrated that cardiotoxicity is often associated with cisplatin treatment.[4]

Cisplatin induces oxidative stress through several mechanisms such as ROS production[5], mitochondrial dysfunction[6], depletion of antioxidants[6], and activation of stress signaling pathways[7], which contributes to cisplatin-induced toxicity and side effects.

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According to Deavall *et al*,[5] excessive free radical production and the high degree of oxidative stress caused by cisplatin may have a significant role in causing oxidative cardiac injury. According to Wozniak *et al*,[8] the medication can produce reactive oxygen species like superoxide anion and hydroxyl radical. Through the action of superoxide dismutase (SOD), the production of superoxide anion can eventually result in the synthesis of hydrogen peroxide (H_2O_2).[9] A significant contributing factor to the development of cardiomyopathy and heart failure, according to Doroshow and Esworthy,[10] is the generation of H_2O_2 above the capacity of the heart to detoxify itself. In this regard, antioxidant-rich diets may be essential for protecting the heart from cardiac damage caused by chemotherapy.

Nuts are nutrient-dense foods with a variety of culinary applications and health advantages. A balanced diet that includes a range of nuts can improve general health and wellbeing.[11] Incorporating a variety of nuts into one's diet has been linked to improving arterial health and lowering inflammation that is linked to heart disease. Nuts offer vital nutrients like vitamin E, folate, and fiber. They also contain a variety of bioactive substances that are thought to play a role in their beneficial effects on cardiovascular health, such as flavonoids, proanthocyanidins, and phenolic acids, in addition to monounsaturated and polyunsaturated fatty acids (like omega-3 and omega-6). Research findings suggest that individuals who consume nuts more than four times a week tend to experience fewer fatal coronary heart disease events in comparison to those who consume them less frequently.[12] Cashew nut, scientifically known as *Anacardium occidentale L.*, is not only delicious but also nutritious nut, making it a valuable addition to various cuisines and diets worldwide. It is advised to be an integral part of a well-balanced diet.[13]

Furthermore, studies have shown that women who regularly include nuts in their diet have a reduced risk of both fatal and non-fatal myocardial infarction.[14] Also, based on prospective research involving male physicians in the United States, it was observed that men who integrated nuts into their diet two or more times weekly had a decreased likelihood of experiencing sudden cardiac death and various forms of coronary heart disease compared to those who rarely or never consumed nuts.[15] An analysis of how cashew nut consumption affected people with metabolic syndrome revealed that it increased their antioxidant capacity.[16] Because of this, the main goal of this study was to look into the potential protective effects of a diet that is enriched with cashew nuts (*Anacardium occidentale L.*) on important biochemical markers of cardiac function in cisplatin-induced cardiotoxic male rats.

Materials and Methods

Chemicals

The following materials were acquired from Sigma Chemical Co. in St. Louis, Missouri, in the United States: adenosine, N-(l-naphthyl) ethylenediamine dihydrochloride, sulphanilamide, cis-diamineplatinum (II) dichloride, p-nitrophenylphosphonate, bovine serum albumin, nitrate, and vanadium chloride (VCl3). Glass-distilled water was used, and all other reagents, such as ferric sulfate, Tris buffer, and thiobarbiturate (TBA), were of analytical quality.

Plant material and sample preparation

The seeds of cashew nuts (*Anacardium occidentale L.*) were purchased in February, 2022 in Erekesan market, Ado – Ekiti (with coordinates 7 0 37 1 N and 5 0 15 1 E), Nigeria. To extract the nuts from the shells, cashew kernels were manually cracked. The nuts were baked for two hours at 100 degrees celsius. To achieve cream-colored nuts, the testa that covered the nuts were squeezed off. Prior to examination, the nuts were ground into flour using a Kenwood blender and placed in a refrigerator and kept there until use in an airtight container. Additionally, the sample was subjected to proximate analysis (Table 1)[17] to find out how many calories were in the nut that was utilized to formulate the diet (Table 2).

Animals

For the study, 36 adult male rats weighing 200–250 g were obtained from the Central Animal House at the College of Medicine at Ekiti State University in Ado, Ekiti, Nigeria. The National Council for Animal Experiments Control (CONCEA) regulations and the institutional ethical committee were followed when handling the animals. Throughout the trial, the animals were housed in stainless steel cages, kept in a room with a 12-hour light/dark cycle, and given free access to food and drink. The environment was maintained at 23 ± 1°C

Experimental protocol and diet formulation

The rats were randomly separated into six groups of six animals and allowed to acclimate for two weeks (n = 6). Group I: Rats in the control condition, fed a standard diet (Skimmed milk (40%), vitamin premix (4%), corn starch (46%), cholesterol free oil (10%) as major constituents, Table 2); Group II: Subjected to a basal diet while being administered cisplatin; Group III were cisplatin-induced rats given diets supplemented with 10% processed cashew nuts (Skimmed milk (31.3%), vitamin premix (4%), corn starch (48.99%), cashew nut (10%), cholesterol free oil (5.17%) as major constituents, Table 2); Group IV indicates cisplatin-induced rats given diets supplemented with 20% processed cashew nuts (Skimmed milk (22.6%), vitamin premix (4%), corn starch (51.98%), cashew nut (20%), cholesterol free oil (1.42%) as major constituents, Table 2); Group V indicates healthy rats given diets containing 10% processed cashew nuts (Skimmed milk (31.3%), vitamin premix (4%), corn starch (48.99%), cashew nut (10%), cholesterol free oil (5.17%) as major constituents, Table 2); Group VI includes healthy rats given diets containing 20% processed cashew nuts (Skimmed milk (22.6%), vitamin premix (4%), corn starch (51.98%), cashew nut (20%), cholesterol free oil (1.42%) as major constituents, as shown in Table 2. The rats in groups II, III, and IV were induced with a single i.p. injection of cisplatin at 7 mg/ml/kg body weight following a 14-day pre-treatment with a cashew nut-supplemented diet.

Table 1: Proximate component of roasted cashew nut

Components	%
Moisture	4.33 ± 0.03
Ash	2.14 ± 0.10
Crude fat	40.32 ± 0.24
Crude protein	25.48 ± 0.12
Crude fibre	3.50 ± 0.04
Carbohydrate	24.23 ± 0.10
PEF %	64.45
PEP %	18.22
PEC %	17.33
UEDP %	10.93
Caloric value (KJ/100g)	2,377.23 ± 0.46

Results represent mean ± standard deviation of three determinations. PEP = Proportion of total energy due to protein, PEF = Proportion of total energy due to fat, PEC = Proportion of total energy due to protein, UEDP = Utilizable energy due to protein. Source: Akomolafe *et al.*, 2022.

Table 2: Diet formulation for basal and supplemented diets for control and test groups.

Treatment	Group I	Group II	Group III	Group IV	Group V	Group VI
Skimmed milk	40.0	40.0	31.3	22.6	31.3	22.6
Oil	10.0	10.0	5.71	1.42	5.71	1.42
Vitamin premix	4.0	4.0	4.0	4.0	4.0	4.0
Corn starch	46.0	46.0	48.99	51.98	48.99	51.98
Cashew nut	-	-	10.0	20.0	10.0	20.0
Total	100g	100g	100g	100g	100g	100g

Note: Skimmed milk = 32% protein; The vitamin premix (mg or IU/g) h was the following composition; 3200 IU vitamin A, 600 IU vitamin D3, 2.8 mg vitamin E, 0.6 mg vitamin K3, 0.8 mg vitamin B1, 1 mg vitamin B2, 6 mg niacin, 2.2 mg pantothenic acid, 0.8 mg vitamin B6, 0.004 mg vitamin B12, 0.2 mg folic acid, 0.1 mg biotin H2, 70 mg choline chloride, 0.08 mg cobalt, 1.2 mg copper, 0.4 mg iodine, 8.4 mg iron, 16 mg manganese, 0.08 mg selenium, 12.4 mg zinc, 0.5 mg antioxidant. Group I: (Control) normal control rats fed basal diet; Group II: (Induced) serve as cisplatin group placed on a basal diet; Group III: cisplatin-induced rats fed diet supplemented with 10% processed cashew nut Group IV: cisplatin-induced rats fed diet supplemented with 20% processed cashew nut; Group V: normal rats fed diet supplemented with 10% processed cashew nut; Group VI: normal rats fed diet supplemented with 20% processed cashew nut.

The rats were sacrificed 24 hours after receiving a cisplatin injection, and daily feed consumption was recorded. Blood from the inferior vena cava of the heart was collected into ethylenediaminetetraacetic acid-containing tubes without protease inhibitors and centrifuged at 3000 g for 15 minutes to produce plasma for biochemical examination.

Necropsy

The hearts of the rats were delicately dissected, cleaned in ice-cold saline, weighed, and then homogenized in the proper buffer while they were still alive. The homogenate was centrifuged for 10 min at 5000 g to separate the homogenate into a low-speed supernatant (S1) and a pellet that was discarded after analysis.[18]

Analysis of activities

The hearts of the rats were delicately dissected, cleaned in ice-cold saline, weighed, and then homogenized in the proper buffer while they were still alive. The homogenate was centrifuged for 10 min at 5000 g to separate the low-speed supernatant (S1) from the pellet, which was then discarded after being used for further investigation. The supernatant so obtained was assayed for adenosine deaminase,[19] monoamine oxidase (MAO),[20] acetylcholinesterase and butyrylcholinesterase,[21] phosphodiesterase-5,[22] arginase,[23] SOD,[24] catalase,[25] GST,[26] and GPx,[27] activities as well as total thiol,[28] non-protein thiol,[28] total antioxidant capacity (TAC),[29] reactive oxygen species (ROS),[30] nitric oxide,[31] and thiobarbituric acid reactive species (TBARS),[32] levels. According to Lowry *et al*.,[33] the heart tissue's total protein content was ascertained.

Results and Discussion

The cardiac tissue is rich in cholinergic nerves, according to several studies[34 - 36]. These nerves must be able to release acetylcholine (ACh) to stimulate the production of NO from L-arginine through the catalytic action of neuronal nitric oxide synthase (nNOS), which is present in both cardiac myocytes and nerve fibers. This will allow the cardiac pump to function and protect the heart as best it can.[34 - 36] Plasma and heart acetylcholinesterase and butyrylcholinesterase activities of cisplatin-induced rats increased significantly when compared to the control rats (Figure 1A and B). However, pre-treatment with dietary supplementation of cashew nuts caused a significant decrease in the acetylcholinesterase and butyrylcholinesterase activities when compared with the induced group.

The rise in AChE and BChE activities in cisplatin-induced groups may support the drug's cardiotoxicity. However, both normal and cisplatin-induced cardiotoxic rats showed a reduction in AChE activity in response to dietary cashew nut treatment. This suggests that there may be the possibility of unlimited bioavailability of acetylcholine in the diet supplemented fed rats. According to recent studies,[37 - 39] increasing levels of ACh can be beneficial in heart failure, but decreasing levels of ACh secretion can lead to heart dysfunction.

The adenosinergic system is crucial for mediating intrinsic and determining myocardial resistance to injury,[40] a purine nucleoside called adenosine is a cardioprotectant that can reduce ischemia insult-induced cellular death and dysfunction. As a result, diminished heart function may result from decreased levels of this cellular messenger.[40] Adenosine deaminase activity in the plasma and heart was increased in the cisplatin-induced group when compared with the control group. In the diet-supplemented cisplatin groups the activity of ADA was decreased compared to the cisplatin-induced group but were not up to control level as presented in Figure 1C.

In this investigation, dietary cashew nut supplementation decreased the activity of this enzyme in both normal and cisplatin-induced rats, whereas the treatment of cisplatin increased the activity of adenosine deaminase (ADA) in the heart tissue. Adenosine's cardioprotective properties may be affected by the up-regulation of ADA.[41] Interstitial adenosine levels rise when ADA which catalyzes the production of inosine from adenosine, is inhibited, possibly inducing tissue protection. It has been reported that inhibition of ADA raises the quantity of adenosine, which subsequently lessens stunning and necrosis in mouse hearts.[42-43]

The results obtained for plasma and heart monoamine oxidase activity were presented in Figure 1D. As can be observed, plasma and heart MAO activity was significantly ($p < 0.05$) increased in the cisplatin-induced group when compared to the control group. Pre-treatment with cashew nut caused a significant ($p < 0.05$) decrease in the plasma and heart MAO activities when compared to the cisplatin-induced group. The inhibition of monoamine oxidases (MAOs) is important for proper functioning of the heart. Cardiovascular dysfunction and oxidative stress are prevented by MAO inhibition. MAOs are flavoenzymes located within the outer mitochondrial membrane, responsible for the oxidative deamination of neurotransmitters and dietary amines.

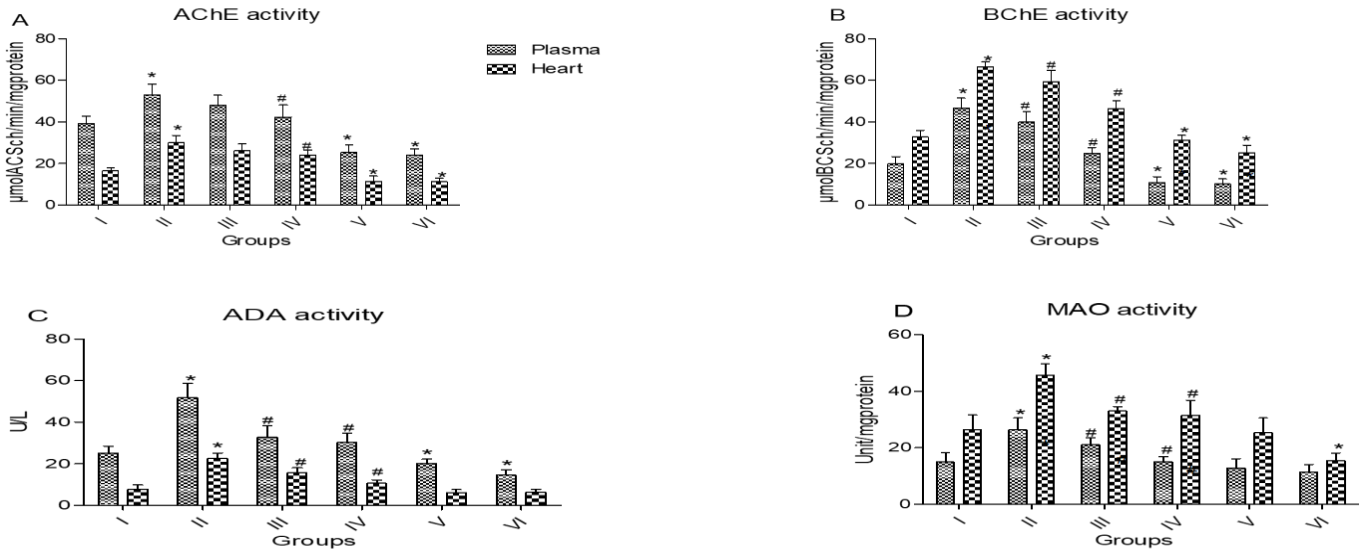

Figure 1: Inhibition of (A) Acetylcholinesterase (AChE), (B) Butyrylcholinesterase (BuChE), (C) Adenosine deaminase (ADA) and (D) Monoamine oxidase activities by diet supplemented with processed cashew nut in cisplatin-induced male rat.

Data are presented as mean ± SEM (n = 6).*Statistically different from control, #from cisplatin-induced group ($p < 0.05$). Group I (normal control rats fed basal diet), Group II (cisplatin-induced rats fed basal diet), Group III (cisplatin-induced rats fed diet supplemented with 10% processed cashew nut), Group IV (cisplatin-induced rats fed diet supplemented with 20% processed cashew nut), Group V (rats fed diet supplemented with 10% processed cashew nut) and Group VI (rats fed diet supplemented with 20% processed cashew nut)

According to several studies,[44-47] the stimulation of MAO activity in the heart is a significant myocardial source of H_2O_2 production that can cause ischemic reperfusion injury and cell death in heart failure. This study shows that cisplatin elevated MAO activity in the heart tissue. Cardiotoxicity has been linked to cisplatin therapy in previous investigations.[48] However, in both healthy and cisplatin-induced rats, pre-treatment with cashew nuts reduced the rise in MAO activity.

The reduction in MAO activity in the rats' heart tissue may be related to the activity of particular phytoconstituents present in the nut. Numerous significant therapeutic drugs have been discovered as a result of reports that phytochemicals have the capacity to alter the physiologically significant activities of essential enzymes.[49] The most significant of these phytochemicals are the polyphenols, which have a wide range of biological activities and potent antioxidant properties. Therefore, the observed decrease in MAO activity in rats fed diets enriched with cashew nuts may be explained by the inhibitory/reductive action of the polyphenolics found in cashew nuts. Previous research has demonstrated the inhibitory effect of certain flavonoids and polyphenols on MAO activity.[50-51]

Endothelial nitric oxide synthase (eNOS) is an enzyme that primarily converts L-arginine into nitric oxide (NO). Endothelial dysfunction, which is linked to congestive heart failure, is characterized by malfunction in the generation and/or bioavailability of NO.[52] Arginase activity in smooth muscle cells and vascular endothelia of cardiac tissue can use L-arginine to lower NOS activity and, as a result, decrease the concentration of NO, a key component of myocardial relaxation and diastolic function.[53-54] In this study, plasma and heart arginase activity of cisplatin-induced rats increased significantly when compared to the control rats (Figure 2A). However, pre-treatment with dietary supplementation of cashew nut caused a significant decrease in the arginase activity when compared with cisplatin-induced group. Whereas, nitric oxide (NO) levels in the plasma and heart were decreased in cisplatin-induced group when compared with the control group. In the diet-supplemented cisplatin group the levels of NO were clearly elevated compared to the cisplatin-induced group as presented in Figure 2C.

Nitric oxide (NO) levels in the cisplatin-induced group decreased as compared to the control group, as shown in figure 2C, supporting the reported considerable increase in arginase activity in cisplatin-induced rats. This finding might support the drug's cardiotoxicity. The cisplatin treatment's inhibition of eNOS activity, which favors the arginase pathway, may be the cause of the rise in arginase activity. According to studies, increasing cardiomyocyte arginase activity may worsen heart failure by reducing NOS signaling.[55] Additionally, Boswell-Smith *et al*.[56] found that individuals with severe heart failure had considerably greater levels of arginase activity compared to control people. Additionally, arginase activity was significantly reduced both under normal condition and in cisplatin-induced rats fed diets supplemented with cashew nuts, and NO levels rose at the same time. Nuts are a good source of L-arginine. The reduction in arginase activity caused by cashew nuts may be an additional therapeutic target for the management of cardiac dysfunction, since this could increase the bioavailability of L-arginine and contribute to the production of NO.[57] This would improve the pace at which the heart's chambers fill with blood for the next beat and enable the heart's muscle to relax more quickly.

Heart failure is a direct result of poor cardiac muscle relaxation, which is caused by the up-regulation of PDE-5. According to Boswell-Smith *et al*.,[56] PDE-5 catalyzes the breakdown of cGMP and lowers NO levels in endotheial cells, which then inhibits signaling. Intraperitoneal administration of cisplatin resulted in a significant increase in the PDE-5 activity in the plasma and heart of cisplatin-induced rats when compared with control rats. However, pre-treatment with dietary supplementation of cashew nut caused a significant decrease in the PDE-5 activity when compared with cisplatin-induced rats (Figure 2B). Cisplatin in this investigation boosted PDE-5 activity in cardiac tissues as well as plasma. But in both healthy and cisplatin-induced rats, pre-treatment with cashew nuts reduced the rise in PDE-5 activity. In the fed rats, this inhibition may hasten cardiac relaxation by cGMP activation, which in turn may result in diastolic function. According to studies, inhibiting PDE-5 may enhance cGMP activity, which may prevent adrenergic, hypertrophic, and proapoptotic signaling in the myocardium.[58-59]

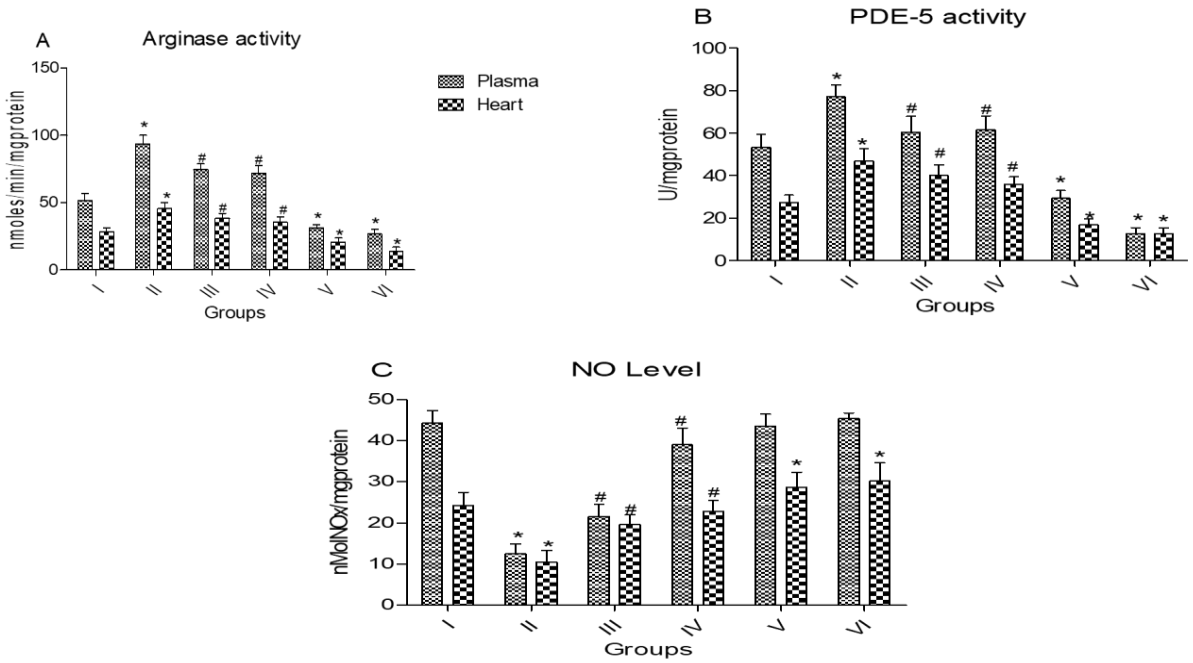

Figure 2: Inhibition of (A) Arginase activity, (B) Phosphodiesterase-5 (PDE-5) activity and the (C) level of nitric oxide (NO) in cisplatin-induced male rats fed with diet supplemented with processed cashew nut. Data are presented as mean ± SEM (n = 6).*Statistically different from control, #from cisplatin-induced group ($p < 0.05$). For details see the legend of Figure 1.

To keep the control of normal heart function in check, the cardiovascular system's antioxidant defense mechanism and ROS formation must coexist in balance.[60] In addition, we saw an imbalance in the cisplatin-induced rats' cardiac tissue and plasma between the antioxidant defense system and ROS production. According to studies by Sabri *et al*.,[60] Sawyer *et al*.,[61] and Cesselli *et al*.,[62] oxidative stress has been associated to cardiac dysfunction. The antioxidant status of the plasma and heart in normal and cisplatin-induced rats is presented in Figure. 3, 4 and 5. Intraperitoneal administration of cisplatin resulted in a significant decrease in the SOD, CAT, GST, GPx activities as well as in TAC, GSH, and T-SHs levels with concomitant elevation in the ROS and TBARS production in the plasma and heart of cisplatin-induced rats when compared with control rats. However, pre-treatment with dietary supplementation of cashew nut caused a significant increase in the SOD, CAT, GST, GPx activities as well as in TAC, GSH and T-SHs levels with a decrease in the ROS and TBARS production when compared with cisplatin-induced rats.

In the cisplatin-induced rats, there was a considerable increase in the formation of ROS and TBARS in cardiac tissue and plasma, as well as a concurrent decline in GST, SOD, CAT, and GPx activities, as well as TAC, GSH, and TSH levels. These findings may indicate that the heart tissue's antioxidant level is insufficient to effectively reduce the induction of oxidative stress in the provoked rats. The increased production of ROS and TBARS in the cardiac tissue of cisplatin-induced rats showed the damage caused by oxidative stress. These results support past research that found a connection between cisplatin treatment and cardiac tissue oxidative stress.[63-64] Overusing GSH may result from excessive TBARS production from lipid peroxidation. The present study revealed a reduction in GSH and T-SH levels, and GST activity in heart tissue. The reduction in GST activity observed in the heart tissue of rats treated with cisplatin may be attributed to either a decrease in substrate GSH or increased blockage by free radicals. The drop in GSH levels points to overuse of the detoxification process as a defense against oxidative stress. Contrarily, cashew nut supplementation effectively prevented the decrease in GST activity, GSH, and TSH levels, which resulted in a noticeable drop in the levels of ROS and TBARS in the plasma and cardiac tissue of cisplatin-induced rats. This finding might be explained by the protective function of phytochemicals found in cashew nuts.[65] Additionally, the nut's antioxidant properties and capacity to prevent lipid peroxidation[65] may offer a way to avoid the production of oxidative stress in the heart tissue of rats given cisplatin treatment.

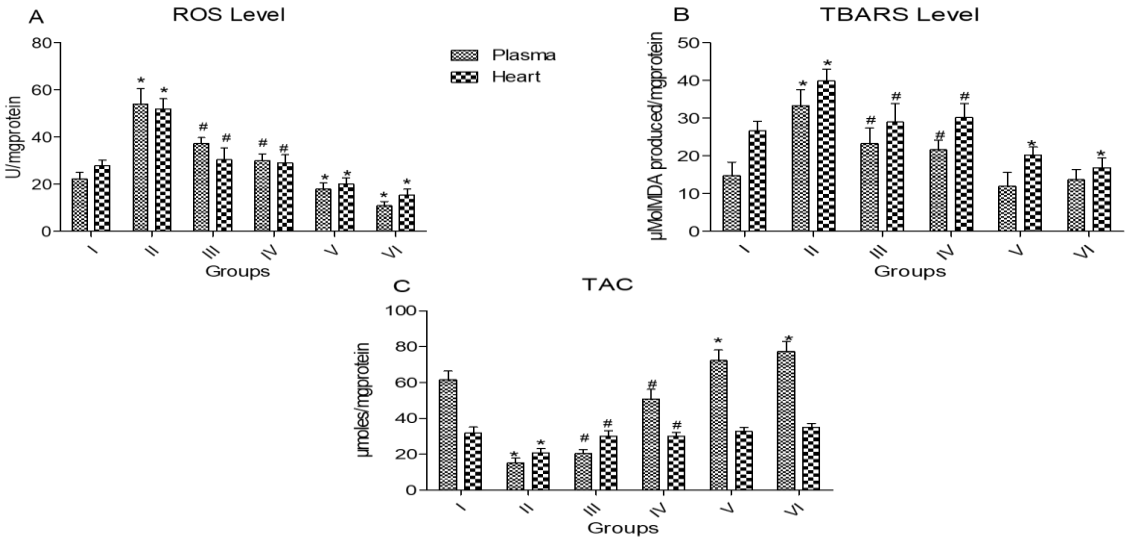

Figure 3: The level of (A) reactive oxygen species (ROS), (B) thiobarbituric acid reactive substances (TBARS) and (C) total antioxidant capacity (TAC) in cisplatin-induced male rats fed with diet supplemented with processed cashew nut. Data are presented as mean ± SEM (n = 6).*Statistically different from control, #from cisplatin-induced group ($p < 0.05$). For details see the legend of Figure 1.

Under Hematoxiline and Eosine staining (X400), in the control group, the cardiac tissue structures were normal (Figure 6I). A similar pattern was found in groups pre-treated with 10% and 20% cashew nut (Figure 6V and VI). Some degenerative changes were observed in the cisplatin-treated group such as severe lesions including myofibrillar loss and vacuolization of cytoplasm and irregularity of myofibrils (Figure 6II). The incidence of these degenerative changes was reduced by the pre-treatment with 10% cashew nut-supplemented diet induced with cisplatin (Figure 6III) while pre-treatment with 20% cashew nut-supplemented diet induced with cisplatin showed a total recovery similar to the control group (Figure 6IV). Under normal condition, the pre-treatment with a diet supplemented with cashew nuts led to a normal histological structure in the heart cells and nuclei. The findings under cisplatin-induced conditions demonstrated that 10% cashew nut pre-treatment reduced heart damage, whereas 20% supplementation resulted in complete recovery up to control level. These results support the study of Wang *et al*.[66] who found that cisplatin-treated rats had histologically worsened cardiac function and myocardial damage. This defense provided by the nut may be a result of its capacity to lessen the buildup of free radicals produced after cisplatin therapy.

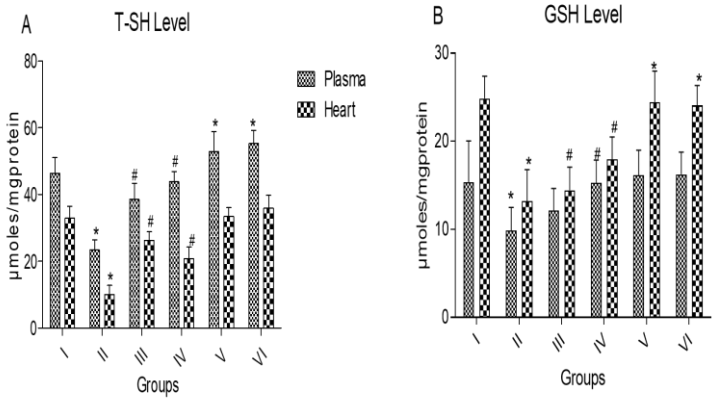

Figure 4: The level of (A) total thiol (T-SH) and (B) reduced glutathione (GSH) in cisplatin-induced male rats fed with diet supplemented with processed cashew nut. Data are presented as mean ± SEM (n = 6).*Statistically different from control, #from cisplatin-induced group ($p < 0.05$). For details see the legend of Figure 1.

Conclusion

The study's findings showed that cisplatin induction caused cardiac dysfunction via altering the activity of the enzymes AChE and BuChE, PDE-5, arginase MAO, and ADA as well as the antioxidant status of the heart and plasma. However, the changes in the aforementioned parameters caused by cisplatin were restored when cashew nuts were added to the diet. Additionally, the heart histological abnormality caused by cisplatin is largely restored by pre-treatment with the prescribed diet. Therefore, we can suggest that the nut could be harnessed as functional foods to prevent cisplatin-mediated cardiac dysfunction.

Conflict of Interest

Authors declare no conflict of interest

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

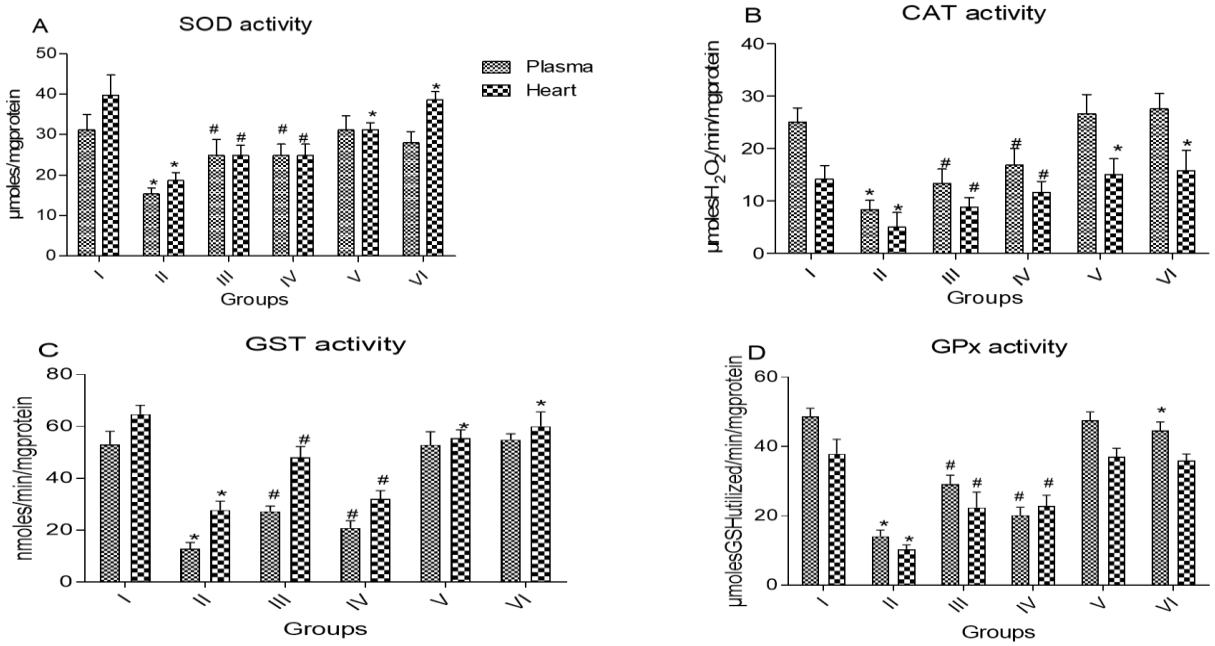

Figure 5: Inhibition of (A) Superoxide dismutase (SOD), (B) Catalase, (C) Glutathione-S-transferase (GST) and (D) Glutathione peroxidase (GPx) activities by diet supplemented with processed cashew nut in cisplatin-induced male rat. Data are presented as mean ± SEM (n = 6).*Statistically different from control, #from cisplatin-induced group ($p < 0.05$). For details see the legend of Figure 1.

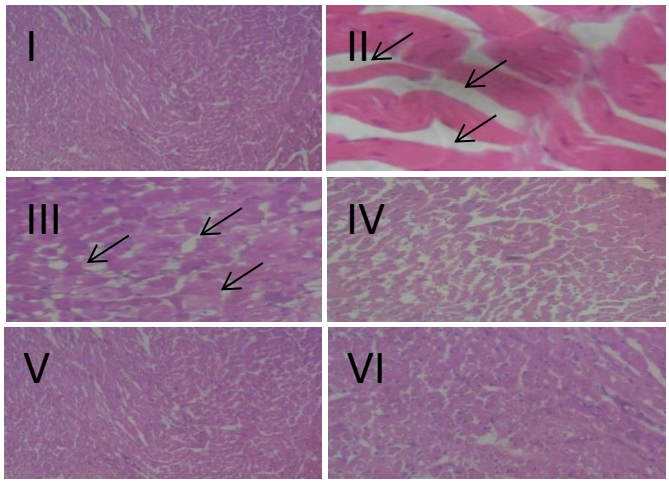

Figure 6: Cardiac tissue photomicrographs of: (I) normal control rats fed basal diet section showing single, oval and centrally located nuclei of cardiomyocytes with regularly arranged cardiac myofibres, (II) cisplatin treated rats fed basal diet section showing severe lesions including myofibrillar loss and vacuolization of cytoplasm and irregularity of myofibrils, (III) cisplatin-induced rats fed diet supplemented with 10% processed cashew nut section showing fewer severe histological changes compared to cisplatin-treated group, (IV) cisplatin-induced rats fed diet supplemented with 20% processed cashew nut section showing a similar pattern to control group, (V) rats fed diet supplemented with 10% processed cashew nut section showing a similar pattern to control group and (VI) rats fed diet supplemented with 20% processed cashew nut section showing a similar pattern to control group.

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