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*Research Article*

# Elevated levels of Cardiac and Oxidative Stress Biomarkers were Ameliorated by Treatment with *Cucumis sativus* Aqueous Extract in Cadmium-Induced Toxicity in Male Wistar Rats

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**ABSTRACT**

**Background**:Cardiovascular diseases are the leading cause of mortality worldwide and cadmium as one of the environmental toxicants contributes adversely to cardiac damage. Hence, this study investigated the cardioprotective potential of *Cucumis sativus* on cadmium-induced toxicity in male Wistar rats.

**Method:** Porcine Sixteen rats weighing between 100 and 180g were grouped with four (A to D) four rats each. Group A was control, Group B-D received 1.5mg/kg bw of cadmium, cadmium + 1mg/kg bw of *C. sativus*, cadmium +2mg/kg bw of C. sativus respectively. Administration was done orally using gavage for 14 days. IBM SPSS statistical software version 28, was used to analyze the data (P-value=<0.05).

**Results:** Lactate dehydrogenase significantly ($p<0.01$) increased in cadmium untreated compared to control and decreased in *C.sativus* treated groups compared to cadmium untreated. Troponin T in cadmium untreated and *C.sativus* (1mg/kg) significantly ($p<0.001$) increased than control. Calcium and Potassium ions in cadmium untreated and *C.sativus* (1mg/kg) significantly ($p<0.001$) increased compared to control and decreased in *C.sativus* treated groups compared to control and cadmium untreated group. Cardiac-reduced glutathione (GSH), glutathione peroxidase (GPx), and catalase in all treated groups significantly ($p<0.001$) decreased compared to control. Although, there was a significant increase in *C.sativus* treated groups compared to cadmium untreated. Superoxide dismutase (SOD) in cadmium untreated and *C. sativus* (1mg/kg) significantly ($p<0.001$) decreased compared to control. However, the *C. sativus* (2mg/kg) group significantly ($p<0.001$) increased compared to cadmium untreated and *C. sativus* (1mg/kg) treated group. Malondialdehyde (MDA) in all treated groups significantly increased compared to the control.

**Conclusion:** It Treatment with C. sativus ameliorated the cardiac toxicity induced by cadmium. Hence, if these results apply to humans, using C. sativus for managing cardiac diseases and oxidative stress should be encouraged as it may possess cardioprotective properties.

## 1. Introduction

Cardiovascular diseases are the leading cause of mortality worldwide. Cardio-protection involves mechanisms and means that contribute to the preservation of the heart by reducing or even preventing myocardial damage (Kübler, 1996). Identifying natural potential therapies for managing cardiovascular diseases is of great interest. *Cucumis sativus* (Cucumber), is a member of the gourd family (Cucurbitaceae), which comprises 98 genera and 975 species of food and ornamental plants. It is one of the oldest cultivated vegetable crops in nearly all countries of temperature zones. It is a thermophilic and frost-susceptible plant species, growing best at temperatures above 20 °C (Tatlioglu, 1993).

Medicinal plants are used to prepare many drugs, but the phytochemical compounds present in original plant material are more efficient with fewer side effects than their pharmaceutical derivatives. Various plants and their bioactive phytoconstituents are well known for their minimal side effects, providing alternative therapeutic potential against cardiac diseases (Tatlioglu, 1993). *Cucumis sativus* are low in calories and fat while being a good source of dietary fiber (Ware, 2019). This combination and their high water content can contribute to maintaining a healthy weight and managing cardiovascular health. The fiber in cucumbers can help regulate cholesterol levels by reducing low-density lipoprotein (LDL) or "bad" cholesterol. Additionally, *Cucumis sativus* contains compounds like cucurbitacins and lignans that may possess cardio-protective properties, including antioxidant and anti-inflammatory effects (Ugwu and Suru, 2021). These properties could help reduce cardiovascular disease risk (Ugwu and Suru, 2021).

Cadmium (Cd) is one of the toxic heavy metals in the environment, which induces oxidative stress, dyslipidemia, and membrane disturbances in the heart (Nazimabashir *et al.,* 2015). It is naturally occurring in the environment as a pollutant that is derived from agricultural and industrial sources. Exposure to cadmium primarily occurs through the ingestion of contaminated food and water and, to a significant extent, through inhalation and cigarette smoking. Cadmium accumulates in plants and animals with a long half-life of about 25–30 years (Genchi *et al., 2020*). Many different forms of exposure to cadmium have been shown over the past century, with cadmium being present in the environment as a result of many human activities (Rahimzadeh *et al.,* 2017). Hence, this study investigated the cardioprotective potential of *Cucumis sativus* on cadmium-induced toxicity in male Wistar rats.

## 2. Methods

Procurement of Test Substance

**2.1 Chemicals:** The cadmium chloride was purchased from Sigma-Aldrich Limited Germany with EC number 233-296-7. Xylazine and ketamine (Guangzhou JHD Chemical Reagent Co., Ltd. Shantou Guangdong, China).

### 2.2 Extraction of *Cucumis sativus*

Firm and dark green colored Cucumber fruits were harvested upon maturity from farmland at IkotAbasi local government area of Akwa Ibom state, Nigeria. It was ensured that they were free from any blemishes or bruises that could affect the quality of the extract. The fruits were washed thoroughly with clean water to remove dirt. Thereafter, cucumber fruits were chopped into tiny pieces using a food processor to increase the surface area and facilitates the release of the contents. After this, the chopped cucumber pieces were immersed in 250ml of distilled water and heated to boiling point for 30 minutes, and then the suspension was filtered using a Whatman filter paper and concentrated using a vacuum evaporator (Labotech International Co., Ltd, Tokyo, Japan) at a temperature of 60 °C (Kumar *et al.*, 2010).

### 2.3 Laboratory Animals

Sixteen (16) male Wistar rats weighing between 100 to 180g were employed for this study. The animals were housed in the Department of Physiology Animal House, University of Calabar, Nigeria. Normal animal cages (435 x 290 x 150mm) with wood flakes as bedding were used in housing the animals (4 rats per cage). They were given ad libitum access to feed (AEC Agrosystem limited, PortHarcourt, Rivers State,

Nigeria) and fresh water, and exposed to 12/12-hr dark/light phase. They were acclimatized for 7 days and kept in line with laid-down ethics for animal care approved by the National Committee for Research Ethics in Science and Technology (NENT), 2018. Before the commencement of this research, ethical approval was obtained from the University of Calabar animal ethics committee, which aligned with the standard guidelines for the use of laboratory animals outlined by the National Committee for Research Ethics in Science and Technology (NENT), 2018. The University of Calabar animal ethics committee permitted the study with ethical clearance registration reference number 040PHY3719.

**2.4 Experimental Design and Administration of Cadmium and *Cucumis sativus***

The animals were arbitrarily allotted into 4 separate groups (n = 4). At the end of 7 days of acclimatization, a solution of Cadmium with a density of 1.5mg/kg was given ad-libitum to induce Cd toxicity in the experimental animals for 4 days. Thereafter, *Cucumis sativus* aqueous extract administration commenced. The Cd and *Cucumis sativus* extract was given via oral means using gavage, once, daily, to animals in treatment groups (2 to 4), using the doses outlined in Table 1, while the control group was given feed and 0.5ml normal saline as a vehicle throughout the experimental period. *Cucumis sativus* aqueous extract administration lasted for fourteen (14) days. However, the rats were euthanized under xylazine and ketamine anesthesia. Blood samples were collected from rats via ocular puncture and the hearts of each rat were harvested. Blood and tissue samples were stored at -80°C until biochemical analyses were performed.

**Table 1. Experimental design and Treatments**

| Groups | No of rats | Treatment |
|---|---|---|
| **Group A (control)** | 4 | Feed + 0.5ml of normal saline as a vehicle throughout the experiment |
| **Group B (cadmium control)** | 4 | 1.5mg/kg bw of Cadmium |
| **Group C** | 4 | 1.5mg/kg bw of cadmium + 1mg/kg bw of *Cucumis sativus* |
| **Group D** | 4 | 1.5mg/kg bw of cadmium +2mg/kg bw of *Cucumis sativus* |

**2.5 Cardiac Biomarkers Assessment**

**2.5.1 Estimation of Lactate dehydrogenase**

Rat specific Lactate dehydrogenase ELISA Kit (E-EL-R2547) was used to determine the concentration of Lactate dehydrogenase using the method described by Freyer and Harms (2017). Principle: By measuring the per-time absorbance reduction at 340 nm, the activating reaction of pyruvate + NADH + H LDA> L-LACTATE + NAD + LDH in the sample is determined.

**Procedure:** Test tubes were carefully categorized and 1ml of the prepared reagent was introduced into the tubes and mixed with 0.02 ml of the sample. Incubate for 60 minutes at 37°C after transferring to the culture. The sample extinction decrease was read at 340 nm at time 0, 60, 120, and 180 cal E/min.

**2.5.2 Estimation of Troponin T**

Rat-specific cardiac Troponin T ELISA Kit (E-EL-R0151) was used to determine the concentration of troponin T using the method of Jaffe *et al.*, (2006). Principle: A specific antibody to Troponin T is immobilized on a microplate. The sample was added to the wells and incubated,

allowing Troponin T to bind to the capture antibody. After washing to remove unbound materials, a detected antibody branded with an enzyme, such as horseradish peroxidase (HRP) was added. The detection antibody recognizes a different epitope on the Troponin T molecule. After another incubation and washing step, a substrate solution was added that reacted with the enzyme, creating a measurable indication directly proportional to the concentration of Troponin T in the sample.

**Procedure:** The supernatant of the homogenized heart was used. The sample was collected into an EDTA tube and centrifuged to obtain serum used for Troponin T measurement. The sample was diluted using an assay buffer after calibration and was added to appropriate wells of the coated microplates and incubated for 60 minutes at 37°C to allow Troponin T present in the sample to bind to the capture antibody. Then the detection antibody was added to each well and incubated to allow the formation of sandwich complexes. The microplate was thoroughly washed to discard unbound detection antibody-enzyme conjugate. A substrate solution (Tetramethylbenzidine (TMB) was added to the wells and incubated on the plate to allow the enzyme-conjugated detection antibody to react with the substrate to produce a colored product. Thereafter, sulfuric acid was added to stop the enzyme reaction and stabilize the color change and the sample absorbance values were read at 450 nm.

**2.6 Cardiac Antioxidant Assessment**

The heart of each rat was harvested and homogenized using a Potter-Elvehjem homogenizer. Twenty percent (1/5 w/v) of tissue homogenate was placed in 50 mm Tris–HCl buffer (pH 7.4) with 1.15% potassium chloride and centrifuged at 10,000 rpm at 4°C for 10 minutes. The supernatant was obtained for catalase (CAT) assay with hydrogen peroxide as substrate. Reduced Glutathione (GSH) was assayed at 412 nm using the method of Luchese *et al.,* (2009). Glutathione peroxidase (GPx) was assayed using hydrogen peroxide as substrate (Lucchese *et al.,* 2009). Superoxide dismutase (SOD) was assayed using the method described by Misra and Fridovich (1972). Malondialdehyde (MDA) was assessed in thiobarbituric acid reacting substances (TBARS) as explained by Meenakshi, *et al.,* (2007); Okhawa, *et al.,* (1979). Afterward, the mixed reaction generated 0.2 ml of 8.1% sodium dodecyl sulfate, 1.5 ml of 20% acetic acid solution matched to pH 3.5 with sodium hydroxide, and 1.5 ml of 0.8% water solution of thiobarbituric acid was added to 0.2 ml of 10%(w/v) of homogenate. The mixture was moved up to 4.0 ml using distilled water and heated at 95°C for 60 mins. Almost 1.0 ml of distilled water and 5.0 ml of the mixture of n-butanol and pyridine (15:1 v/v) was added and centrifuged ice cooling at 4000rpm. The crude layer was discarded and absorbance was summed at 532 nm and added with results obtained from MDA standards. The concentrations were calculated from absorption values as normal absorption. The method was recently used by Mobisson *et al.,* (2023)

**2.7 Measurement of serum electrolytes**

The serum calcium ion concentration was determined by the o-cresolphthalein complexone method (Baginsky *et al.,* 1973). This method is based on calcium ions reacting with o-cresolphthalein complexone in an alkaline solution to form an intense violet-colored complex.

Procedure: The test tubes (Becton, Dickinson, and Company, USA) were labeled as test, standard, and blank. Thereafter, 1.0 ml of the reagent was introduced into all the test tubes. Then 0.025ml of the samples were added into appropriate tubes and mixed vigorously. The mixture was allowed for 5 minutes, thereafter, the absorbance was read and recorded at 590nm. The increase in absorbance of the mixture is directly proportional to the calcium ion concentration in the sample. The concentration of serum calcium ion was calculated by dividing the absorbance of the test by the absorbance of the standard, multiplied by the concentration of the standard which is 2.5mmol/l.

Serum Potassium ion concentration was determined using Chow *et al.,* (2008) method. Principle: The assay for potassium involves the measurement of the concentration of potassium ions in a sample using an ion-selective electrode.

The ISE consists of a membrane that selectively permits potassium ions to pass through, generating an electrified potential that is proportional to the concentration of potassium ions in the sample. Procedure: Calibrate the ion-selective electrode and place the electrode in the sample, then allow for sufficient time for equilibration, during which the potassium ions in the sample will bind to the sensing elements in the electrode. The electromotive force generated by the electrode was measured using a potentiometer and converted to potassium concentration using the calibration parameters. The measured potassium concentration in the sample was then reported.

**2.8 Statistical analysis**

All results are presented as mean ± SEM, n=4. One-way analysis of variance (ANOVA) was utilized in comparing the differences within groups, followed by post hoc multiple comparisons. Computer software SPSS version 28 and Excel analyzer were used for the analysis. The level of significance was set at $p<0.05$.

## 3. Results

**3.1 Comparison of mean cardiac biomarkers in control and treated groups**

In Table 2 below, the serum lactate dehydrogenase concentration in the cadmium control was significantly ($p<0.01$) increased compared to the control. Groups treated with cadmium+*C.sativus* (1mg/kg) and cadmium+*C. sativus* (2mg/kg) significantly ($p<0.05$) decreased compared to cadmium control. Cardiac Troponin T concentration in cadmium control was significantly ($p<0.001$) increased compared to control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly ($p<0.01$) increased compared to control. Rats treated with cadmium+*C. sativus* (1mg/kg) significantly ($p<0.001$) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly ($p<0.001$) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly ($p<0.001$) decreased compared to cadmium+*C. sativus* (1mg/kg)

**Table 2 Comparison of mean cardiac biomarkers in control and treated groups**

| Parameters | Group A(control) | Group B (Cd control) | Group C (Cd+1mg/kg C.S) | Group D (Cd+2mg/kg C.S) |
|---|---|---|---|---|
| **Lactate dehydrogenase (U/L)** | 21.25±0.47 | 34.00±5.06** | 23.00±0.40[a] | 18.50±0.64[f] |
| **Troponin T (Pg/ml)** | 37.50±1.04 | 60.00±1.08*** | 45.50±0.64**, [c] | 36.25±2.98[g, ##] |

Values are expressed as mean ± SEM, n=4, **=p<0.01, ***=p<0.001 vs control, a=p<0.05 vs cadmium, c= p<0.001 vs cadmium, f= p<0.01 vs cadmium, g= p<0.001 vs cadmium, ## = p<0.001 vs cadmium + CS (1mg/kg).

**3.2 Comparison of mean serum electrolyte concentration in control and treated groups**

In Table 3 below, Calcium ion concentration in the cadmium control was significantly ($p<0.001$) increased compared to the control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly ($p<0.05$) increased compared to control. Rats treated with cadmium+*C. sativus* (1mg/kg) significantly ($p<0.01$) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly ($p<0.001$) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly ($p<0.05$) decreased compared to cadmium+*C. sativus* (1mg/kg). Serum Potassium ion concentration in the cadmium control was

significantly (p<0.001) increased compared to control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly (p<0.01) increased compared to control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly (p<0.05) decreased compared to control. Rats treated with cadmium+*C. sativus* (1mg/kg) significantly (p<0.001) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.001) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) decreased compared to cadmium+*C. sativus* (1mg/kg).

**Table 3 Comparison of serum electrolyte concentration of control and experimental groups.**

| Parameters | Group A(control) | Group B (Cd control) | Group C (Cd+1mg/kg C.S) | Group D (Cd+2mg/kg C.S) |
|---|---|---|---|---|
| Calcium (mmol/L) | 3.07±0.04 | 3.62±0.04*** | 3.30±0.07*, b | 3.07±0.04g, # |
| Potassium (mmol/L) | 4.75±0.06 | 6.00±0.09*** | 5.52±0.08**, a | 4.30±0.21*, g, ### |

Values are expressed as mean ± SEM, n=4, *=p<0.05, **=p<0.01, ***=p<0.001 vs control, a= p<0.001 vs cadmium, b= p<0.01 vs cadmium, g= p<0.001 vs cadmium, # = p<0.05, ### = p<0.01 vs cadmium + CS (1mg/kg),

**3.3 Comparison of mean cardiac oxidative stress markers in control and treated groups**

In Table 4 below, Cardiac reduced glutathione concentration in all treated groups significantly (p<0.001) decreased compared to the control. Group treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) increased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) increased compared to cadmium+*C. sativus* (1mg/kg). Cardiac glutathione peroxidase concentration in all treated groups significantly (p<0.001) decreased compared to control. Group treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) increased compared to cadmium control. Rats treated with cadmium+C. sativus (2mg/kg) significantly (p<0.01) increased compared to cadmium+*C. sativus* (1mg/kg). Cardiac catalase concentration in all treated groups significantly (p<0.001) decreased compared to the control. Group treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.001) increased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.001) increased compared to cadmium+*C. sativus* (1mg/kg). Cardiac superoxide dismutase concentration in cadmium control and cadmium+*C. sativus* (1mg/kg) significantly (p<0.001) decreased compared to control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly (p<0.01) increased compared to cadmium control. Group treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.001) increased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) increased compared to cadmium+*C. sativus* (1mg/kg). Cardiac malondialdehyde concentration in all treated groups significantly increased compared to control. Group treated with cadmium+*C. sativus* (1mg/kg) significantly (p<0.05) decreased compared to cadmium control. Rats treated with cadmium+*C. sativus* (2mg/kg) significantly (p<0.01) decreased compared to cadmium+*C. sativus* (1mg/kg).

**Table 4 Comparison of mean cardiac oxidative stress markers in control and treated Groups**

| Parameters | Group A(control) | Group B (Cd control) | Group C (Cd+1mg/kg C.S) | Group D (Cd+2mg/kg C.S) |
|---|---|---|---|---|
| GSH ug/ml | 1.44±0.10 | 0.57±0.04*** | 0.07±0.01*** | 0.96±0.04***, f, ## |
| GPx ug/ml | 0.06±0.00 | 0.02±0.00*** | 0.02±0.00*** | 0.04±0.00***, f, # |
| CAT u/g | 0.91±0.02 | 0.36±0.00*** | 0.36±0.01*** | 0.52±0.01***, g, ### |
| SOD ug/ml | 0.36±0.01 | 0.20±0.01*** | 0.27±0.00***, b | 0.34±0.01g, ## |
| MDA umol/ml | 0.34±0.04 | 0.55±0.01*** | 0.46±0.02**, a | 0.43±0.01*, f |

Values are expressed as mean ± SEM, n=4, *=p<0.05, **=p<0.01, ***=p<0.001 vs control, a= p<0.001 vs cadmium, b= p<0.01 vs cadmium, f= p<0.01 vs cadmium, g= p<0.001 vs cadmium, # = p<0.05, ## = p<0.01, ### = p<0.001 vs cadmium + CS (1mg/kg).

**4. Discussion**

The significant increase in lactate dehydrogenase concentration in treated groups compared to control may likely indicate cardiac damage induced by cadmium administration (Arora *et al.,* 2017). However, the *Cucumis sativus* treated groups significantly reduced compared to the cadmium untreated group. This reduction may be linked to the ameliorative effect of *Cucumis sativus* (Olaniyan *et al.,* 2019). Ugwu and Suru, (2021) reported that *Cucumis sativus* contains cucurbitacins and lignans that may possess cardio-protective properties, including antioxidant and anti-inflammatory effects (Ugwu and Suru, 2021). Lactate dehydrogenase is an enzyme that converts lactate to pyruvate in the anaerobe's metabolic pathway. The group administered with cadmium was higher compared to the control group, indicating cellular damage or stress (Paul *et al.,* 2010). This may be linked to the disruption of cellular processes by cadmium and this may cause oxidative stress (Ognjanovic *et al.,*2008).

Troponin T is a protein and serves as a biomarker for cardiac injury, the result showed that the group administered with cadmium was higher compared to the control. This may likely be due to compromised cardiac muscle cells (Eldin and Hafez, 2016). Cadmium exposure is known to be harmful to various organs including the heart, liver, and kidney (Kiran-Kumar *et al.,*2016). This led to oxidative stress, cellular damage, and inflammation. The significant decrease in the *Cucumis sativus* treated group compared to cadmium control could be due to the cardio-protective effect of *Cucumis sativus* (Ugwu and Suru, 2021). There was a significant increase in the concentration of calcium and potassium ions in treated groups compared to the control. This may be due to cadmium exposure influencing calcium metabolism or uptake in the body. Disrupted calcium homeostasis induced by cadmium results in cell apoptosis, autophagy, or tumorigenesis (Choong *et al.,* 2014; Zhou *et al.,* 2015). The significant decrease in the Cucumis sativus treated group compared to the cadmium control could be due to the cardio-protective effect of Cucumis sativus. The reduction in cardiac glutathione levels in the cadmium-treated group compared to the control may be due to

cadmium's toxic effects on cells. The reduction in glutathione could impair the cells' ability to defend against oxidative damage, potentially impacting cardiac health (Benedetta *et al.*,2007). The groups that were administered cadmium had significantly lower levels of cardiac glutathione peroxidase compared to that of the control group, this is due to cadmium's toxic effects on enzyme activities (Ognjanovic *et al.*,2008). The oxidative stress in rats can also be applied to humans. Cadmium exposure might lead to decreased enzyme activities which then results in lower levels of glutathione peroxidase in the heart tissues (Benedetta *et al.*,2007). There was a significant decrease in cardiac catalase concentration treated groups compared to the control. This could be cadmium's toxic effect on cellular processes, including oxidative stress (Ognjanovic *et al.,* 2013). This could lead to the reduction in catalase activity and concentration, contributing to oxidative damage in the heart tissue. Cardiac superoxide dismutase was significantly lowered compared to control. The reduced concentration of superoxide dismutase in treated groups may likely be due to the toxic effect of cadmium on cellular processes, leading to reduced enzyme functions or expression (Mobisson *et al.*,2023). Malondialdehyde concentration was significantly higher in the treated groups compared to the control. Its higher level in cadmium-treated groups may be an indication of increased oxidative damage (Benedetta *et al.,* 2007). Malondialdehyde is a maker of lipid peroxidation, which tends to increase when cells are exposed to elevated levels of oxidative stress (Meenakshi *et al.,* 2007).

## 5 Conclusions

Administration of cadmium caused a significant increase in cardiac biomarkers (Lactate Dehydrogenase and Troponin T), Ca2+, K+, decreased antioxidant activities, and increased lipid peroxidation by causing increased MDA concentration. Treatment with Cucumis sativus had ameliorative effects. Hence, moderate consumption of *C. sativus* should be encouraged as it may possess cardio-protective potential.

## 6. Declarations

### 6.1 Ethics approval

University of Calabar animal ethics committee permitted our research procedure with approval number 040PHY3719.

### 6.2 Availability of data and materials

All data generated or analyzed during this study are included in this article.

### 6.3 Competing interests

There are no competing interests. Each author has read the document and given their consent for publication.

### 6.4 Funding

There was no funding assistance from any private or public sector.

### 6.5 Authors' Contributions

Mobisson Samuel Kelechi designed the study and wrote the study protocol. Mobisson Samuel Kelechi and **Agnes Igimi Odey** performed laboratory experiments and literature searches. Mobisson Samuel Kelechi drafted the manuscript; **Enene Esu Ukpai** worked on data analysis. Mobisson Samuel Kelechi performed the statistical analysis. All authors read and approved the final manuscript.

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