

Investigating The Protective Potentials of Zingiber Officinale Towards Cadmium Induced Damage to The Lungs of Albino Male Wistar Rats

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Abstract

This study was carried out to investigate the protective effects of Zingiber officinale in cadmium-induced lung damage. Twenty (20) adults male Wistar rats were used for this study and the experiment lasted for 21 days. The rats were divided into five groups of four rats each namely; Group 5 (control) given normal diet and distilled water, Group 4 rats were induced with 2mg/kg of cadmium alone, Group 3 received 2mg/kg of cadmium plus 410.8mg/kg of ginger, Group 2 received 2mg/kg of cadmium plus 273.8mg/kg of ginger; Group 1 received 2mg/kg of cadmium plus 136.9mg/kg of ginger. The rats were weighed every first day of the week. On day 21, the rats were sacrificed and the lungs were harvested and fixed immediately in 10% buffered formalin, processed and stained with Harris Haematoxylin and Eosin (H&E) staining solution. Blood samples were collected by cardiac puncture for full blood count analysis. Data were expressed as mean + standard error of the mean (M + SEM) and subjected to one way analysis of variance (ANOVA). 95% level of significance (P<0.05) was used for statistical analysis. Ethanolic extract of Zingiber officinale could not protect the lungs from the toxic effect of cadmium chloride.

Keywords: cadmium; lungs; ginger; wistar rat; damage

1.Introduction

Cadmium (Cd) is a heavy metal that does not have any physiological function and is often considered a toxicant (Aeschbach *et al.*, 1994). The constant sources of cadmium contamination are related to its application in industry as a corrosive reagent, as well as its use as a stabilizer in PVC products, color pigments, and Ni-Cd batteries. Cadmium is also present as a pollutant in non-ferrous metal smelters and the recycling of electronic waste. Activities such as volcanic eruption, erosion and abrasion of rocks and soil, and forest fires are among the reasons for the increase in cadmium concentrations in the living environments. When cadmium enters the body, it is transported to the bloodstream via erythrocytes and albumin and is then accumulated in the kidneys, liver and gut. Ginger (Zingiber officinale) belongs to the family Zingiberaceae and genus Zingiber. Other names of ginger are African ginger, Black ginger, Cochin ginger, GanJiang, Gegibre, Jamaican ginger, and Race ginger. Turmeric, cardamom, and galangal are other notable members of the ginger family (Anandaraj *et al.*, 2001). The English botanist Williams Roscoe gave the plant the name Zingiber, derived from a Sanskrit word singabera which means horn-shaped due to the protrusions of the rhizome. Ginger is a good source of essential micronutrients such as potassium, magnesium, copper, manganese and silicon. Potassium and manganese help to build resistance to diseases and protect the lining of the heart, blood vessels, and urinary passages. Ginger offers many health benefits to the body. Due to its anti-inflammatory qualities, ginger causes bronchodilation in asthmatic patients. Studies have also shown that ginger has various uses including anti-oxidant, anti-cancer, cardio-protective, anti-inflammatory, anti-viral effects. The aim of this study

was to investigate the mitigating effects of ginger extract on histomorphological alterations in the lungs of matured male Wistar rats exposed to cadmium induced toxicity.

2.Materials and Method

2.1 Materials Used

The materials used included twenty adults male Wistar rats, clean wooden cages, water bowls, weighing balance, vital feeds, saw dust, masking tapes, syringe, dissecting set, beaker, dissecting board, sample bottles, normal saline, phosphate buffered formalin, cadmium, ginger extract and distilled water.

2.2 Acquisition of Zingiber officinale

Zingiber officinale was purchased from a local market in Uyo Local Government Area of Akwa Ibom State, Nigeria.

2.3 Plant Extraction

Zingiber officinale were washed, air dried under shade and grinded into fine powder using an electric blender before extraction with ethanol and kept in a bottle with a tight-fitting cover.

2.4 Animal Care and Protocol

Twenty (20) adult male albino Wistar rats weighing between 123g and 222g were used for this study. The rats were acquired from the animal house of

the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo, Nigeria. They were kept in wooden cages with sawdust used as beddings. The animals were given water and a normal rat diet to eat. Five groups with four rodents each were formed from the total number of rats. Groups one through four were the experimental groups, while Group five served as the control group. All animals were handled in accordance with the National Academy of Science's "guide for the care and use of laboratory animals," which was published by the National Institute of Health.

2.5 Acclimatization of Experimental Animals

In strict accordance with the university's animal handling ethics, the animals were housed in wooden cages and suitably acclimatized for a period of two

weeks (14 days) in the animal house of the Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo, Nigeria. Before the experiment began, the rats underwent this acclimatization to help them get used to their new surroundings. Throughout the duration of the study, the rodents were given unlimited access to water and rat food.

2.6 Experimental Design and Administration of Extract and Cadmium

Ginger extract and cadmium were administered orally according to body weight of experimental animals. The animals were classified into five groups (4 rats per group). The experimental regimen is represented in table 1.

Groups	Regimen	
1	2mg/kg of Cadmium plus 136.9mg of <i>Zingiber officinale</i>	21 days
2	and 2mg/kg of Cadmium plus 273.8mg of <i>Zingiber officinale</i>	
3	2mg/kg of Cadmium plus 410.7mg of <i>Zingiber officinale</i>	
4	2mg/kg of Cadmium alone 10ml of distilled water	21 days 21 days

Table 1: Table showing experimental Design

2.7. Determination of Body Weight

The animals were weighed before and after administration prior to sacrifice using an electronic weighing balance. Percentage change in body weight was calculated and recorded as; $\text{Final weight} - \text{Initial weight} / \text{Final weight} \times 100/1$

2.8 Statistical Analysis

Data obtained from the study was expressed as mean \pm standard error of mean and were analysed using one-way analysis of variance (ANOVA) to

determine the difference between the experimental groups and control group using graph prism in version 8.

3. Results

3.1 Result of the Protective Effect of Ginger Extract on the Body Weight of Cadmium-Induced Rats

Result showed that the final body weight of all the treated groups and control was significantly ($p < 0.05$) lower compared to the initial weight.

Groups	Initial Body Weight (g)	Final Body Weight (g)	Percentage Weight (%)
Cadmium + Ginger 136.9 mg/kg	226.0 \pm 5.85	176.8 \pm 9.10 ***	0.90
Cadmium + Ginger 273.8 mg/kg	249.3 \pm 6.29	164.5 \pm 7.96 ***	0.85
Cadmium + Ginger 410.7 mg/kg	227.8 \pm 9.13	172.5 \pm 8.99 ***	0.55
Cadmium alone	256.3 \pm 9.87	187.3 \pm 2.19 ***	0.69
Control	223.8 \pm 2.39	155.3 \pm 3.20 ***	0.69

Values are expressed in Mean \pm SEM

*** indicates significant difference from Initial body weight @ $P < 0.05$

Table 2: Effect of Ginger Extract on Body weight of Cadmium-Induced Rats.

3.2 Effect of Ginger Extract on Lung Weight of Cadmium-Induced Rats

Results showed that there was no significant difference in the lung weight of all the treated groups compared to control.

Groups	Kidney Weight (g)
Cadmium + Ginger 136.9 mg/kg	1.21 \pm 0.10
Cadmium + Ginger 273.8 mg/kg	1.10 \pm 0.03
Cadmium + Ginger 410.7 mg/kg	1.42 \pm 0.21
Cadmium alone	1.12 \pm 0.11
Normal Control	0.99 \pm 0.08

Values are expressed in Mean \pm SEM and non significant @ $P < 0.05$

Table 3: Effect of Ginger Extract on Lung Weight of Cadmium-Induced Rats

3.3 Effect of Ginger Extract on Haematological Indices of Cadmium-Induced Rats

Results showed that haemoglobin (Hb) and red blood cells (RBC) levels was not significantly different in all the treated groups compared to the control

(Table 4). However, white blood cells (WBC) level was significantly ($p < 0.05$) higher in cadmium plus ginger 410.7 mg/kg group compared to control and other treated groups, respectively (Table 4). Platelets (PLT),

PCV, MCV, MCH and MCHC showed no significant difference in all the treated groups compared to control, respectively (Table 4 & 5).

Groups	Hb (g/dl)	RBC ($\times 10^9 \mu\text{l}$)	WBC ($\times 10^3 \mu\text{l}$)	PLT ($\times 10^3 \mu\text{l}$)
Cadmium + Ginger 136.9 mg/kg	12.55 \pm 0.31	7.56 \pm 0.26	3.80 \pm 0.48	677.5 \pm 13.38
Cadmium + Ginger 273.8 mg/kg	10.90 \pm 1.14	6.56 \pm 0.49	4.70 \pm 0.48	784.0 \pm 74.00
Cadmium + Ginger 410.7 mg/kg	10.18 \pm 1.39	5.83 \pm 0.97	9.20 \pm 0.58***	807.5 \pm 62.96
Cadmium alone	13.40 \pm 0.49	7.68 \pm 0.19	5.13 \pm 0.40	819.0 \pm 59.23
Normal Control	12.75 \pm 0.56	7.28 \pm 0.31	5.30 \pm 0.50	580.5 \pm 26.10

Values are expressed in Mean \pm SEM and non significant @ $P < 0.05$

*** indicates significant difference from control and other treated groups @ $P < 0.05$

Table 4: Effect of Ginger Extract on Haematological Indices of Cadmium-Induced Rats

Groups	PCV (%)	MCV (fL)	MCH (pg)	MCHC (g/dl)
Cadmium + Ginger 136.9 mg/kg	48.43 \pm 0.53	65.68 \pm 1.29	25.85 \pm 0.43	25.85 \pm 0.47
Cadmium + Ginger 273.8 mg/kg	41.65 \pm 4.94	65.75 \pm 0.71	26.33 \pm 0.45	26.33 \pm 0.46
Cadmium + Ginger 410.7 mg/kg	38.98 \pm 5.77	67.80 \pm 2.19	26.28 \pm 0.38	26.28 \pm 0.38
Cadmium alone	52.08 \pm 1.70	67.80 \pm 1.29	25.15 \pm 0.28	25.15 \pm 0.27
Normal Control	57.44 \pm 2.93	67.00 \pm 1.35	26.20 \pm 0.61	26.20 \pm 0.61

Values are expressed in Mean \pm SEM and non significant @ $P < 0.05$

Table 5: Effect of Ginger Extract on Haematological Indices of Cadmium-Induced Rats

3.4 Haematoxylin and Eosin (H&E) Method for General Demonstration of Lung

In figure I, transverse section of the lungs of Wistar rats given 2mg/kg of cadmium plus 136.9mg/kg (low dose) of ginger for three weeks showed abnormal respiratory histo-structure with perivascular and neutrophilic inflammatory cells infiltration and pulmonary blood vessels within the alveolar interstitium. The lungs were moderately affected. The transverse section of the lungs of Wistar rats given 2mg/kg of cadmium plus 273.8mg/kg (medium dose) of ginger for three weeks indicated abnormal respiratory histo-structure with widespread atrophying pneumocytes and pulmonary blood vessels within the alveolar interstitium. Lung tissues were moderately affected (figure II). In figure III, the transverse section of the

lungs of Wistar rats given 2mg/kg of cadmium plus 410.7mg/kg (high dose) of ginger for three weeks revealed abnormal respiratory histo-structure with widespread fibrosis of the alveolar interstitium, presence of terminal bronchiole and pulmonary blood vessels within the alveolar interstitium. The transverse section of the lungs of Wistar rats given 2mg/kg of cadmium alone for three weeks disclosed abnormal respiratory histo-structure with widespread fibrosis of the alveolar interstitium, presence of terminal bronchiole with its surrounding cartilage (figure IV). In figure V, the transverse section of the lung of the Wistar rats given distilled water for three weeks unveiled normal architecture of the tissue consisting of alveolar cells and capillaries, inter alveolar septa, alveolar sacs and macrophages. The cells and tissues of the lung were intact.

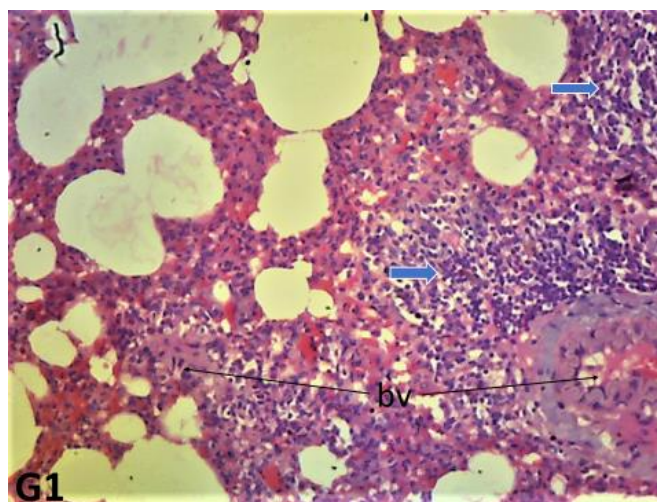


Figure I: Photomicrograph of the transverse section of the lungs of male Wistar rats given 2mg/kg of cadmium plus 136.9mg/kg (low dose) of ginger for three weeks showing abnormal respiratory histo-structure with perivascular and neutrophilic inflammatory cells infiltration (blue arrow) and pulmonary blood vessels (bv) within the alveolar interstitium. (x100)

Inference: Moderately affected.

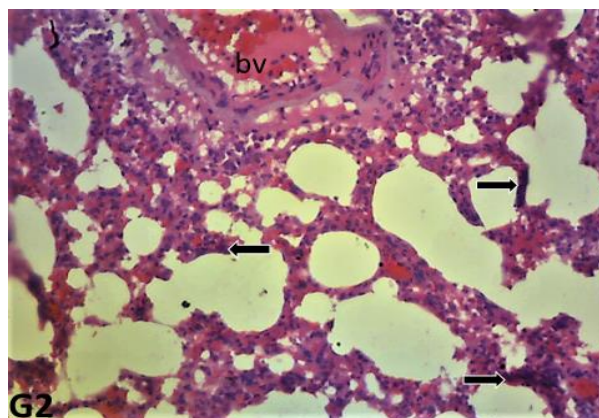


Figure II: Photomicrograph of the transverse section of the lungs of male Wistar rats given 2mg/kg of cadmium plus 273.8mg/kg (medium dose) of ginger for three weeks showing abnormal respiratory histo-structure with widespread atrophying pneumocytes (black arrow) and pulmonary blood vessels (bv) within the alveolar interstitium. (x100)

Inference: Moderately affected.

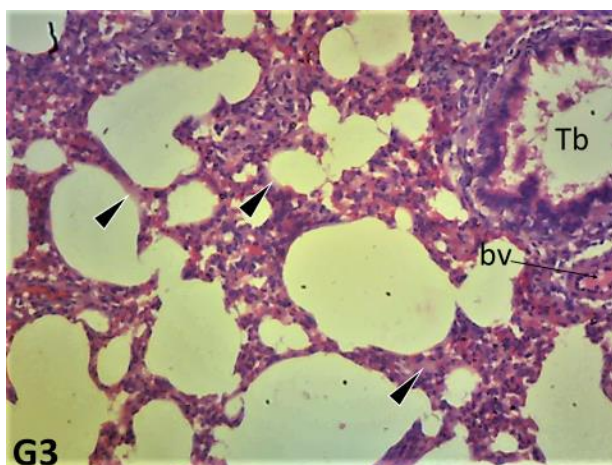


Figure III: Photomicrograph of the transverse section of the lungs of male Wistar rats given 2mg/kg of cadmium plus 410.7mg/kg (high dose) of ginger for three weeks showing abnormal respiratory histo-structure with widespread fibrosis of the alveolar interstitium (arrow head), presence of terminal bronchiole (Tb) and pulmonary blood vessels (bv) within the alveolar interstitium. (x100)

Inference: Moderately affected.

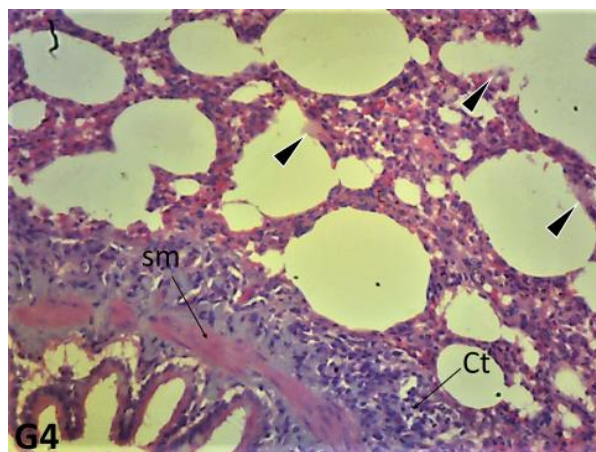


Figure IV: Photomicrograph of the transverse section of the lungs of male albino Wistar rats given 2mg/kg of cadmium alone for three weeks showing abnormal respiratory histo-structure with widespread fibrosis of the alveolar interstitium (arrow head), presence of terminal bronchiole with its surrounding cartilage (Ct) within the alveolar interstitium.

Inference: Moderately affected.

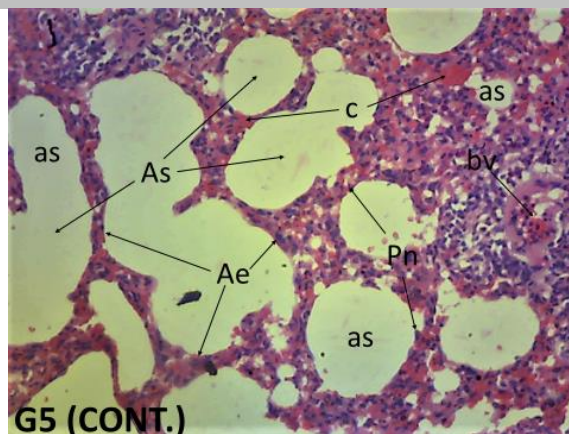


Figure V: Photomicrograph of the transverse section of the lungs of male Wistar rats given 10ml of distilled water (Control) showing normal respiratory histo-architecture with normal presentation of air space (As) within the alveolar sacs (as), pneumocytes (Pn) and capillaries (c) within the alveolar interstitium and blood cells (Bv) within the blood vessels (Bv). (x100)

Inference: Not affected.

4.0 Discussion

As far back as the 16th century, cadmium has been known to be present as a pollutant in non-ferrous metal smelters and the recycling of electronic waste as a result of many human activities and is often considered a toxicant. In this present study, the doses of cadmium consumed by the experimental animals showed a significant decrease in the final weight of animals in all groups throughout the period of administration. Cadmium can interfere and substitute for the essential micronutrients and also induce oxidative stress. Deficiency of these essential elements can reduce adiposity in rats thereby resulting in a weight loss (Miguel *et al.*, 2010). Weight loss could lead to dizziness, constipation, hair loss, fatigue, muscle loss and muscle cramps, low energy as well as dehydration and electrolyte imbalance. This corresponds to similar findings which reported a significant difference in the body weights of rats after cadmium administration. Administration of cadmium revealed several histopathologies in the lungs ranging from abnormal respiratory histo-structure, neutrophilic inflammation with fibrosis and atrophy of pneumocytes. This is because cadmium can cause an increased risk of chronic and obstructive lung disease and collapse of the alveoli. Chronic cadmium consumption may also be a possible cause of lung cancer (Sorahan and Esmen, 2004). Other respiratory effects associated with cadmium exposure include bronchitis, rhinitis and destruction of olfactory epithelium with resultant formation of anosmia (ATSDR, 1999; Drebler, 2002). From our findings, administration of cadmium relatively caused subtle changes in the lungs. WBC was significantly increased in the cadmium group, this may be due to the fact that, WBC are involved in the body's defense mechanism and cadmium toxicity elicited an influx of WBC components into blood to cushion the toxic effects. Our findings corroborated similar findings which reported that cadmium exposure can result in a variety of adverse effects, such as renal and hepatic dysfunction and pulmonary edema. Epidemiological study reveals that chronic exposure of cadmium can lead to lung carcinogenesis with an increased production of reactive oxygen species which will lead to destruction of various molecules such as enzymes, nucleic acid and membrane phospholipids (Alessia *et al.*, 2020). Cadmium has been reported to produce obvious signs of atrophic changes in the lungs of animals. The absorption of cadmium takes place mainly through the respiratory tract and to a smaller extent via the gastrointestinal tract. When cadmium enters the body, it is transported to the bloodstream via erythrocytes and albumin and is then accumulated in the kidneys (Satarug, 2018). This indicates that cadmium has serious harmful effects on the micro-architecture of the adult Wistar rats. Ginger is a potential herb used worldwide for its immense phytotherapeutic properties. In Ayurveda it is known to improve body functions and helps to eliminate toxins from the body (Natta *et al.*, 2008). Modern scientific research has revealed that ginger possesses numerous therapeutic properties including antibiotic, antimicrobial, and antioxidant effects, an ability to inhibit the formation of inflammatory compounds, and direct anti-inflammatory effects.

Besides this, ginger is also effective against some kinds of cancer, stimulates blood circulation, controls blood pressure and hypertension, helps in lowering cholesterol, and is associated with combating heart problems. Despite all these therapeutic efficacies widely reported to be associated with ginger, it did not actually protect the lungs against cadmium induced damage. This may be connected to several factors such as dosage and time.

5. Conclusion

Results obtained in this study revealed that cadmium is harmful when consumed. However, the study also revealed that *Zingiber officinale* extract exhibited little or no protective effect on the histoarchitecture of the lungs of adult Wistar rats despite having anti-inflammatory and antioxidant properties.

Competing Interest

Authors declare that no competing interests exist.

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