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Recuperative Action of Aqueous *Carica papaya* Extract on Cadmium Induced Loss of Nissl Bodies in the Frontal Cortex

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Authors' contributions

This work was carried out in collaboration between all authors. Authors HBA and ODO designed the study and wrote the protocol. Authors SAA and ARO performed the statistical analysis. Authors KOO, PKO and AAA wrote the first draft of the manuscript. Author FEO managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Cadmium is a heavy metal that causes generation of free radicals that have been discovered to cause damage to cells and tissues in the body. This research work examined the damaging effects of cadmium, and the recuperative effect of *Carica papaya* aqueous extract to restore normal cell functioning.
Methods: 30 Wistar rats (70 g-190 g) were used for this research. The rats were randomly selected into six groups of five animals each. A single dose of $3CdSO_4.8H_2O$ 3 mg/kg body weight were administered intraperitoneally to four of these groups against control group not exposed to

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Cadmium. Two groups were treated with different doses of *Carica papaya* fruit extract for the period of four weeks. A group was given Vit. C and Vit. E as prophylactic treatment. After four weeks, the rats were sacrificed and organ excised, weighed and fixed for histological processing and stained with Cresyl fast violet stain. The photomicrographs of the normal control, induced control and treated groups were observed and compared for changes and differences.

Results: The findings showed that rats damaged with cadmium stained with low Cresyl dye intensive affinity coloration compared to the normal control group indicative of degeneration and loss of Nissl bodies, this suggest possible alteration in protein synthesis necessary for proper cell functioning. While the treated groups showed a higher Cresyl dye intensity affinity of colour.

Conclusion: *Carica papaya* can help restore the presence and functioning of Nissl bodies in the cell.

Keywords: Cadmium; nissl bodies; prefrontal cortex; cresylfast violet.

1. INTRODUCTION

Cadmium is a heavy metal, widely used in industry that causes health problems through occupational and environmental exposure [1]. Non-occupational exposure is mainly from cigarette smoke which contains relatively high concentrations of this element; for non-smokers who are not occupationally exposed, diet is the main route of exposure to cadmium. Reactive oxygen species generated as a result of cadmium exposure interact with many redox sensitive molecules, causing functional disruption and structural changes, and as a secondary messenger, they influence gene regulation. Due to these changes in gene regulation, cadmium-induced elevation of cellular reactive oxygen species may lead to altered production of a wide range of proteins in the cell [1].

Lots of people in various established systems of the world use medicinal plants as an alternative treatment of their diseases; this could be due to how expensive orthodox health care is, or may be as a consequence of the worldwide move towards the utilization of natural, rather than manmade products. Hence, products with antioxidant properties, such as *Carica papaya* have in recent times been given special attention as potential remedial and preventative agents [2]. This research work aimed at investigating the damaging effects of cadmium, and the recuperative effect of *Carica papaya* aqueous extract to restore normal cell functioning in Wistar rats.

2. MATERIALS AND METHODS

2.1 Extract

A mature unripe *Carica papaya* (pawpaw) fruit weighing 1518 grams was purchased from Kuchikau town, Nasarawa state, Nigeria, and taken to the Biology department of Bingham University, Nigeria for authentication. The *Carica papaya* was peeled and the seeds discarded. The *Carica papaya* was cut into pieces and 1000 grams was weighed. The weighed *Carica papaya* was then put in 1000 ml of distilled water. The mixture was left to soak for 72 hours (3 days) at room temperature. After the 72 hours, it was sieved and the residue was weighed. The weight of the residue was 570 g, and the supernatant was 1150 ml. The supernatant was then stored in the refrigerator till when it was needed [3].

2.2 Experimental Design

30 male Wistar rats weighing between 70 g-190 g were used for this research work. The rats were randomly selected into six groups as follows: A, B, C, D, E and F; each group containing five rats. They were kept in the animal house of Bingham University, Nigeria and given water and feed twice daily. The treatment for the various groups was administered accordingly, following strictly, the ethical approval and guides of the ethical committee of College of Health Sciences, Bingham University, Nigeria.

2.3 Administration of Chemical and Treatment

The cadmium stock solution was made by dissolving 10 mg of Cadmium sulphate salt in 5 ml of 0.9% w/v phosphate buffer. The cadmium stock solution was administered intraperitoneally in doses corresponding to the weight of the rats using 1 ml insulin syringes. 250 mg/kg and 400 mg/kg body weight of aqueous *Carica papaya* fruit extracts were administered orally to rats in groups C and D for the period of four weeks and served as treatment groups. 0.5 ml of 0.9%w/v

phosphate buffer was administered to the normal group A control rats and a single dose of 3.0 mg/kg of $3CdSO_4.8H_2O$ was administered to rats in group B (negative control), group E and group F. Group E rats were given Vit. C and E only, while group F were induced with a single dose of $3CdSO_4.8H_2O$ after administering Vit. C and E for 28 days.

2.4 Procedure of Animal Sacrifice

The rats were sacrificed through cervical dislocation. The skulls were dissected and the brains were harvested. The brain tissues were fixed in 40% formal calcium. The tissues were processed and stained with Cresyl fast violet stains to demonstrate Nissl bodies.

3. RESULTS AND DISCUSSION

Cresyl violet demonstrates Nissl bodies which are aggregates of basophilic Rough ER, found in abundance in the neuron soma. Extensive dark purple coloration was observed in the tissue micrograph of the group A animals, indicating the presence of sufficient Nissl bodies in the cells. In a normal cell, the RER functions in the production and modification of proteins that are to be packaged, in addition to the production of membrane lipids and proteins [4].

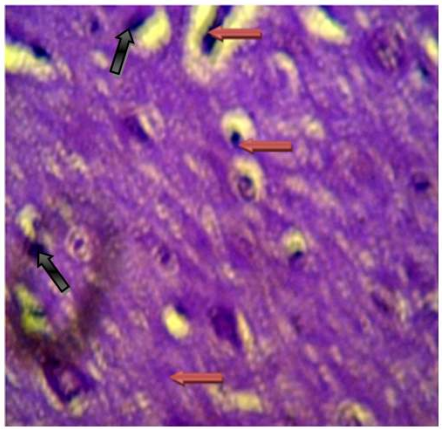

Fig. 1. Normal control group A: The extensive dark purple coloration indicating an abundance of Nissl bodies characteristic of a normal cell. Cresyl violet x400

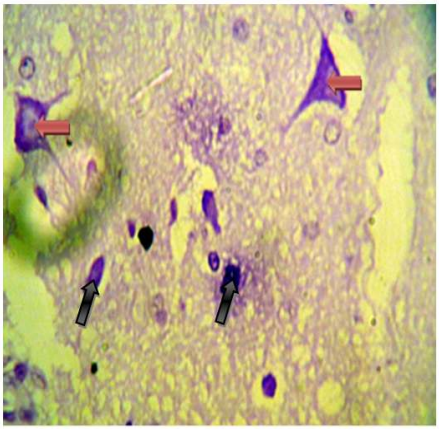

Fig. 2. Induced control group B: Light purple coloration indicating a reduction of Nissl bodies indicating cellular damage. Cresyl violet x400

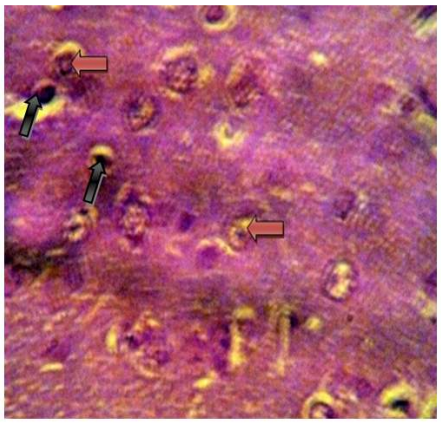

Fig. 3. Treated group C high dose: Extensive dark coloration observed across the tissue, indicating restoration of cell activities. Cresyl violet x400

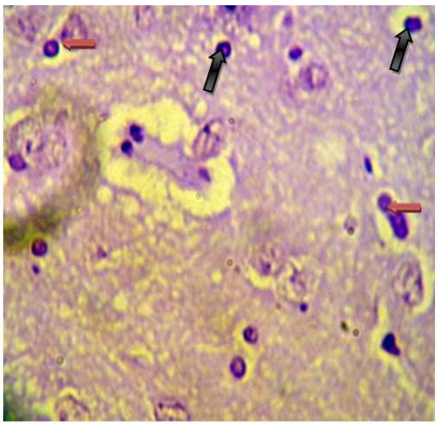

Fig. 4. Treated group D low dose: Dark coloration observed in few cells, indicating gradual repair of cell. Cresyl violet x400

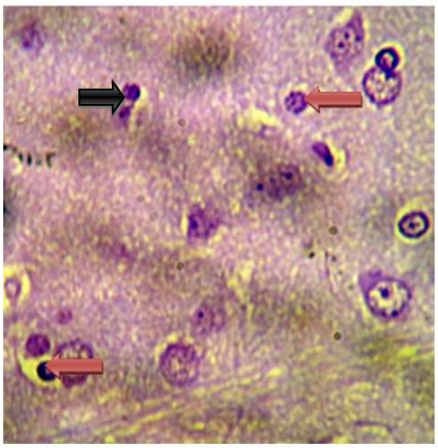

Fig. 5. Prophylactic treatment group E: A reduction in dark purple coloration in the micrograph. Cresyl violet x400

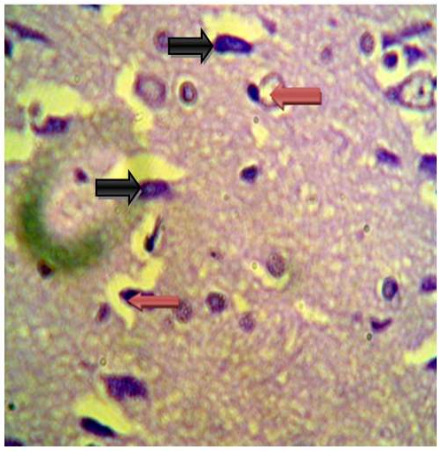

Fig. 6. Positive control group F: Low intensity of purple coloration in the tissue. Cresyl violet x400

Aggregates of Nissl bodies

Neurons

The intensity of the dark purple coloration is greatly reduced which means that there is reduction of the amount of Nissl bodies in the cells and tissue micrograph of group B rats induced with cadmium. This suggests that some function of protein synthesis and packaging is lost in the cells. Heavy metals such as cadmium have been implicated in oxidative damage caused by the increase of ROS and their consequent attack on proteins, lipids, and nucleic acids, leading to failure of functioning of enzymes, distorted membrane fluidity, and genomic damage [5].

Treatment of Group E animals with vitamins C and E, modified the cadmium induced effects on rats, served to protect the tissue. The intensity of the dark purple coloration signifying presence of Nissl bodies in the tissue micrographs of the animals was reduced but the damage was not as widespread as in the group induced with cadmium only. This suggests that water-soluble ascorbic acid (Vit. C) and the water-insoluble α-tocopherol (Vit. E), help to protect against tissue damage due to generation of ROS by cadmium [6]. The ROS are powerful oxidizing agents with the purpose of causing oxidative damage to biomolecules such as lipids and proteins and ultimately causing cell death [7,8].

Studies have shown that papaya fruit has antioxidants that help to reduce oxidative stress by regulating protein biosynthesis [9,10]. This is observed in the group C and group D animals treated with high and low doses of *Carica papaya* extract, with the restoration of extensive dark purple coloration demonstrating numerous Nissl bodies indicating extensive protein synthesis in the cells. Though the groups treated with high dose showed better recuperative effect than the group of rats treated with low dose which suggest that the effects of pawpaw fruit juice are dose dependent. Group F treated with vit. C and Vit. E for the period of four weeks and induced with cadmium showed little on morphological change in the distribution of nissl substance, indicating that they has little or no protective function against Cadmiun toxicity.

4. CONCLUSION

Cadmium causes a considerable reduction in the amount of Nissl bodies in the cells which can affect neuronal function due to inhibition of protein synthesis. This research shows that *Carica papaya* has recuperative action on the Nissl bodies in the cells.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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