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# The Effect of Parkia Leaf Extract on Cadmium-Induced Cerebral Leison in Wistar Rats

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author ODO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author VOM managed the literature searches, analyses of the study performed the spectroscopy analysis and authors OPO and OBF managed the experimental process and authors BJD and SAA identified the species of plant. All authors read and approved the final manuscript.*

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## ABSTRACT

Cadmium is a relatively rare soft metal that occurs in the natural environment typically in association with zinc ores and to a lesser extent, with lead and copper ores. It is highly toxic to both human and animals because it is widely distributed in the environment and is used in various industries. Some of the toxic effects of cadmium exposure are testicular atrophy, renal dysfunction, hepatic damage, hypertension, central nervous system injury and anemia. *Parkia biglobosa* serves as a remedy for quite number of ailments and has medicinal properties against bronchitis, pneumonia, diarrhea, violent colic, vomiting sores and ulcers. This research work was targeted at investigating the activities of cadmium and *Parkia biglobosa* leaf extract on the histoarchitecture and histochemistry in prefrontal cortex. Thirty Wistar rats were used for the study. The animals were acclimatized for two weeks and were maintained under standard condition in Bingham University animal house holding they were housed in well ventilated cages and kept under

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controlled light schedule and were fed with standard laboratory feed and water *ad libitum*. The rats were randomly grouped into six groups A, B, C, D, E, F each containing five animals. Group A served as control, Groups B, C, D, E and F were injected intra-peritoneally with 3.0 mg/kg of cadmium sulphate. After 72hrs of injecting cadmium, group C, D and E were administered orally with 20 mg/kg, 30 mg/kg and 40 mg/kg of the leaves extract of *Parkia biglobosa* respectively and group F received oral administration of 100 mg/kg and 30 mg/kg of vitamin C and E respectively for two weeks. Animals were sacrificed after two weeks of the last administration of the *Parkia biglobosa* leaf extract by cervical dislocation. Cadmium administration caused a significant increase ($P< 0.05$) of LDH, G6PD and MDA level in cadmium group animal while there was a significant decrease in LDH, G6PD and MDA level upon administration of *Parkia biglobosa* leaf extract. This study has shown that *Parkia biglobosa* leaf extract has antioxidant properties that might have enhanced morphological damage caused by cadmium by regenerating pyramidal and neuroglial cells and improving distribution of Nissl bodies in the prefrontal cortex of the treated rats.

*Keywords: Cadmium; prefrontal cortex; parkia and neurons.*

## 1. INTRODUCTION

Environmental pollution associated with heavy metals has been of global concern over many decades [1]. These heavy metals are natural components of the environment but high rate of industrialization has been responsible for their wider diffusion and dispersal in the environment amongst are Lead, Zinc, mercury, Copper [2]. Food contains cadmium as a result of uptake from the soil by plants and bioaccumulation in terrestrial and aquatic animals [3]. Cadmium is also emitted into the atmosphere from natural sources, mainly volcanic activities, and from anthropogenic sources. Long term chronic exposure of cadmium has been associated with anaemia, anosmia, osteomalacia and cardiovascular diseases especially hypertension [4]. Cadmium may induce oxidative damage in different tissues by enhancing peroxidation of membrane lipids in tissues and altering the antioxidant systems of the cells. The peroxidative damage to the cell membrane may cause injury to cellular components due to the interaction of metal ions with the cell organelles [5]. Cadmium depletes glutathione and protein bound sulfhydryl groups resulting in enhanced production of reactive oxygen species such as superoxide ions, hydroxyl radicals and hydrogen peroxides. These reactive oxygen species result in increased lipid peroxidation [6].

The use of herbs to treat disease is almost universal among non-industrialized societies, and is often more affordable than modern pharmaceutical drugs. The World Health Organization (WHO) estimates that 80 percent of the populations of some Asian and African countries presently use herbal medicine treatment of various ailments. Biological compounds present in *Parkia biglobosa* leaves with antioxidant properties contribute to the protection of cells and tissues against deleterious effects of reactive oxygen species and other free radicals. Protective agents from plant origin with anti peroxidative and antioxidant properties play an important role in protecting the liver against toxicity [2,7]. According to [8] aqueous extract of *Parkia biglobosa* leaves induced an increase in both the count of total lymphocytes and TCD4+ in blood therefore, it could help strengthen the immune system of immune-suppressed.

The brain is part of the nervous system. The brain is the major component of the central nervous system [9]. It is a network of more than 100 million individual nerve cells interconnected in systems that control perception and the machinery of action [10]. The prefrontal cortex is the anterior part of the frontal lobes of the brain lying in front of the motor and premotor areas [9]. This brain region has been implicated in planning complex cognitive behavior, personality expression, decision making and moderating social behavior [10]. The basic activity of this brain region is considered to be orchestration of thoughts and actions in accordance with internal goals [11].

The most typical psychological term for functions carried out by the prefrontal cortex area is executive function [12]. Executive function relates to abilities to differentiate among conflicting thoughts, determine good and bad, better and best, same and different, future consequences of current activities, working toward a defined goal, prediction of outcomes, expectation based on actions, and social

"control" (the ability to suppress urges that, if not suppressed, could lead to socially unacceptable outcomes) [11].

Many researchers have indicated an integral link between a person's personality and the functions of the prefrontal cortex [9]. The prefrontal cortex has been defined based on cytoarchitectonics by the presence of a cortical granular layer IV. It is not entirely clear who first used this criterion. Many of the early cytoarchitectonic researchers restricted the use of the term prefrontal to a much smaller region of cortex including the gyrus rectus and the gyrus rostralis [12]. In terms of Brodman areas, the prefrontal cortex traditionally includes areas 8, 9, 10, 11, 44, 45, 46, and 47 (to complicate matters, not all of these areas are strictly granular—44 is dysgranular, caudal 11 and orbital 47 are agranular [13].

## 2. MATERIALS AND METHODS

The plant material was collected from Bingham University, Nigeria and *Parkia biglobosa* leaves were identified by botanist in the department of Biological Science of Bingham University. The plant material was air dried at room temperature for three weeks and grounded into fine powder, which was extracted and screened for phytochemical properties as described by method of [14].

Thirty Wistar rats were used for the study. The animals were made to acclimatize for two weeks and were maintained under standard condition in Bingham University animal house holding, they were housed in well ventilated cages and kept under controlled light schedule (12 hour light and 12 hour dark) cycle and were fed with standard laboratory feed and water *adlibitum*. The rats were randomly grouped into six A, B, C, D, E and F, each containing five animals. Group A served as control, Groups B, C, D, E and F were injected intra-peritoneally with 3.0 mg/kg of cadmium sulphate ($3CdSO4.8H_2O$) [15]. Groups C, D and E were administered orally with 20 mg/kg, 30 mg/kg and 40 mg/kg of the extract respectively 72 hours after injecting cadmium while group F were given vitamin C and E as standard drugs 72 hours after given cadmium as well. An equivalent volume of phosphate buffer was administered to groups A which served as normal control for the period of two weeks.

Animas were sacrificed after two weeks of last administration of the *parkia biglobosa* leaf extract by cervical dislocation. The brain tissues were carefully excised and fixed in 10% formol-calcium for histological preparation while tissue blocks were sectioned at 5 um thick for routine H&E (Haematoxylin and Eosin) and Cresyl fast violet for Nissl bodies and other brain tissues were homogenized in 5% sucrose solution at 4℃ for histochemistry bioassay.

## 3. RESULTS AND DISCUSSION

The phytochemical screening of *Parkia biglobosa* leaf extract revealed bioactive constituents present in the extract such as flavonoid, terpenoids, saponin, tannins, steroid and cardiac glycoside which are antioxidant agent against factors causing inflammation, diabetes, cardiac failure, hypertention, bacterial infection, cancer cells, diarrhea, scurvy and membrane lipid perioxidation as shown in Table 1 and reported by [7]. The above phytochemical findings provide information on the protective functions of *Parkia biglobosa* leaf extract against factors that might have implicated the prefrontal cortex to cause cell damage [8]. There was a lost of weight in cadmium animal group when compare with the initial weight of the same animal group (Table 2) which was reported that there must be loss of appetite and weight as a result of excessive accumulation of Cadmium [6].

**Table 1. The result of the phytochemical analysis of the ethanolic extract of *Parkia biglobosa***

| Compounds | Result |
|---|---|
| Phlobatannins | - |
| Flavonoids | + |
| Alkaloids | - |
| Saponins | + |
| Tannins | + |
| Terpenoids | + |
| Steroids | + |
| Glycosides | + |

*+ Present and – not present*

Observation on the enzymes of carbohydrate metabolism such as LDH and G6PD shows a significant difference in cadmium group as compared with normal control group which suggest a disruption in carbohydrate metabolism pathway and depletion of the antioxidant defense system as evident in cadmium group rats [6] and antioxidant enzyme (MDA) also so similar characteristic, increase in Maleioaldyhyde (MDA) were evident in cadmium group rats as compared with animals in normal control and

other treatment animal groups which is significant, hence, there was an increase in the membrane lipid peroxidation in cadmium group animal which suggest tissue damage [16]. The treatment group animal's shows recuperative evident as a result of antioxidant agents found in *Parkia biglobosa* leaf extracts as shown in Table 3 [17].

The histomorphological and cytological reports revealed distortion, cellular irregularity and chromatolysis as evident in cadmium group animals (Plate B) as compared with animals in the control group (Plate A) with normal morphology and intact cells with their nuclei which were also evident in the treated animals (Plate C- F) as relatively similar as control group animal. Cadmium and *Parkia biglobosa* leaf extract demonstrate deleterious as in the case of Cadmium while *Parkia biglobosa* revealed ameliorative and protective properties respectively in observed in their tissue morphology and Nissl bodies distribution [16].

**Table 2. Weight of Wistar rats before and after experiment**

| Groups' | Initial mean weight (g) | Final mean weight (g) |
|---|---|---|
| Normal control | 176±5.0 | 162±5.8 |
| Induced control (Cadmium) | 148±4.9 | 113.2±5.0 |
| Cadmium + Low dose (Parkia) | 176±11.7 | 184±6.5 |
| Cadmium + Middle dose(Parkia) | 150.4±3.3 | 136±4.0 |
| Cadmium + High dose (Parkia) | 136±4.0 | 105.8±4.4 |
| Cadmium + Vitamin C&E | 208±8.0 | 176.4±6.7 |

*Mean Weight ± SEM (g): The table above shows the mean weight of each group before and after administration of cadmium and the extract*

**Table 3. Prefrontal enzyme histochemistry activity**

| Groups | LDH | G6PDH | MDA |
|---|---|---|---|
| Normal control | 10158±43.0 | 7193±42 | 34.5±1.5 |
| Induced control (Cadmium) | 10314.5±45 | 8707.5±12.5 | 43.5±0.5 |
| Cadmium + Low dose | 10421±11.0 | 7255.5±2.5 | 32±0.0 |
| Cadmium + Middle dose | 11418±16.5 | 9217.5±2.5 | 34.±1.0 |
| Cadmium + High dose | 10338.5±1.5 | 8639±41.0 | 38.5±1.5 |
| Cadmium + Vitamin C&E | 10214.5±9.5 | 7180.5±0.5 | 30.5±0.5 |

*Mean ± SEM (IU/L); a = P≤0.05 compared with control*

**Photomicrograph**

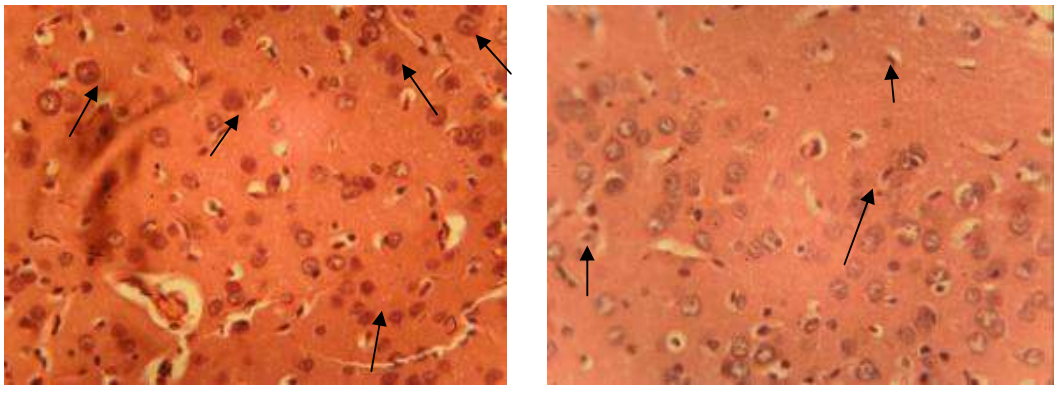

**Plate A** **Plate B**

**Plate A. prefrontal cortex of the control group; numerous intact pyramidal cells with their nuclei while Plate B. prefrontal cortex of the group administered with only cadmium which shows pyramidal neurons distortion and cells with vacuolated cytoplasm. Using H/E X100**

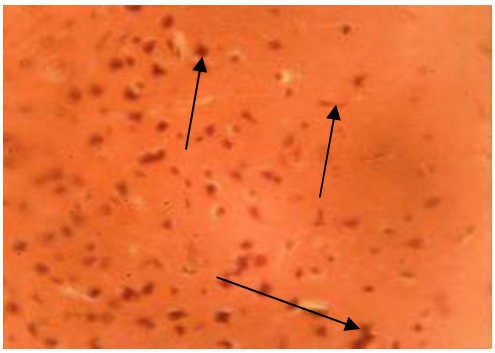

Plate C

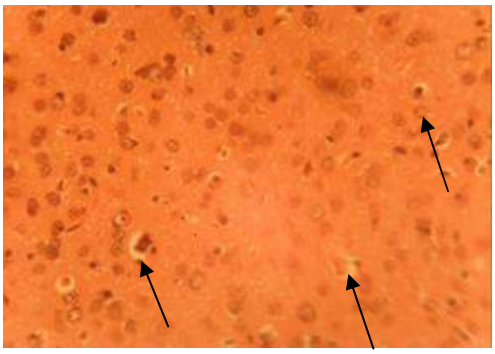

Plate D

**Plate C. prefrontal cortex of the group administered with cadmium + low dose of extract shows irregularly darkly stained pyramidal cells with pyknotic nuclei while Plate D. prefrontal cortex of the group administered with Cadmium + middle dose of extract shows faintly stained pyramidal cells and their nucleus are also faintly stained. Using H/E X100**

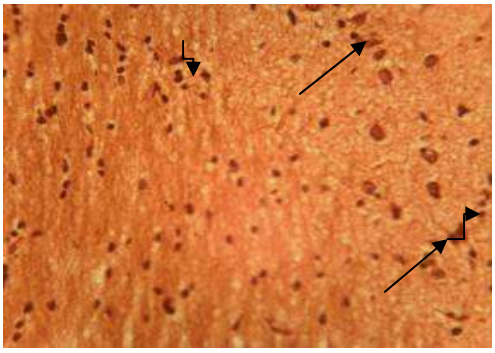

Plate E

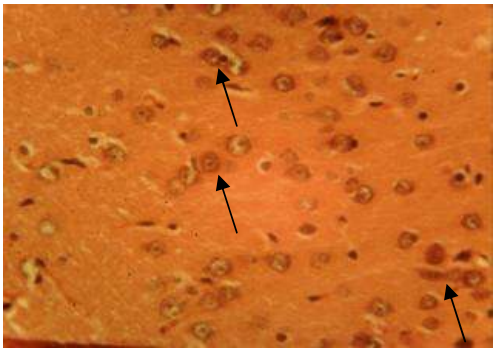

Plate F

**Plate E. prefrontal cortex of the group administered with cadmium + high dose of extract shows numerous neuroglial cells with scanty pyramidal cells and Plate F. prefrontal cortex of the group administered with only cadmium + Vitamin C&E shows pyramidal cells that is not as darkly stained has seen in the normal control group A and with their nuclei. Using H/E X100**

**Cresyl Fast Violet**

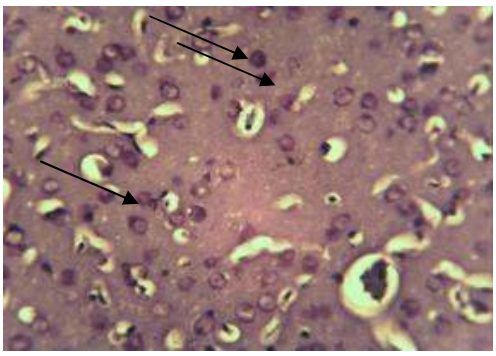

Plate A

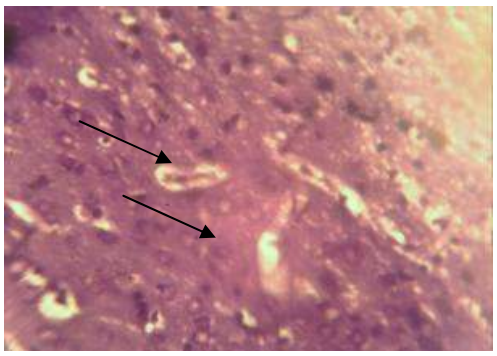

Plate B

**Plate A. prefrontal cortex of the normal control group shows deeply stained photomicrograph which indicates the presence of numerous Nissl substance while Plate B. prefrontal cortex of the group administered with only cadmiumshows fainted staining characteristic of the prefrontal pyramidal cells which suggests loss of Nissl bodies (chromatolysis). Using CFV X100**

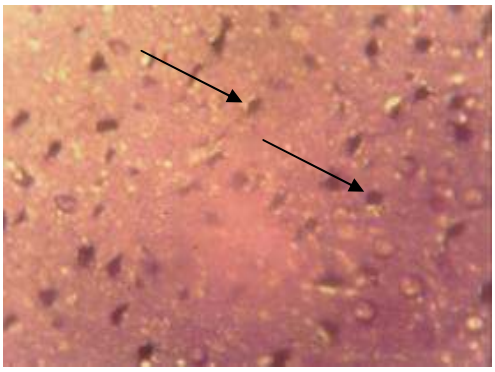

**Plate C**

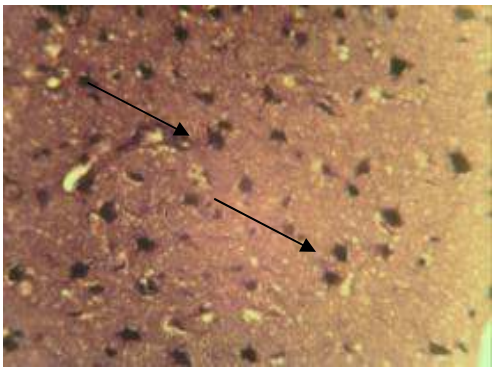

**Plate D**

**Plate C. Prefrontal cortex of the group administered with Cadmium+ low dose of the extract, showing a pale staining characteristic, loss of Nissl bodies was evident while Plate C. prefrontal cortex of the group administered with Cadmium+ middle dose of the extract. Shows a slightly deep stained characteristic of the prefrontal cortex and increased number Nissl bodies. Using CFV X100**

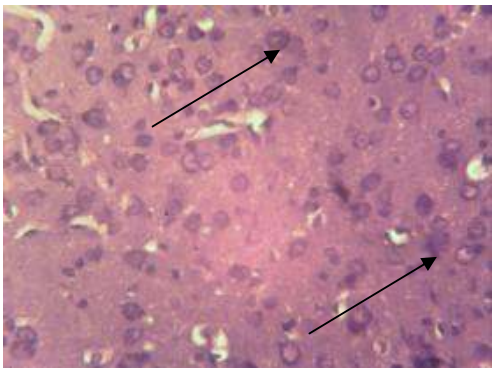

**Plate E**

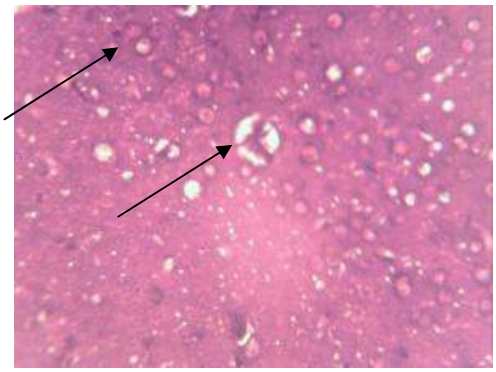

**Plate F**

**Plate E. Prefrontal cortex of the group administered with Cadmium + high dose of the extract shows a deeply stained characteristic of the prefrontal cortex with increase in the Nissl bodies while Plate F. Prefrontal cortex of the group administered with Cadmium + Vitamin C&E shows a pale-blue staining characteristic of the prefrontal pyramidal cells which suggests present of Nissl bodies in a small amount. Using CFV X100**

## 5. CONCLUSION

*Parkia biglobosa* leaf extract was potent in controlling the cellular damage induced by cadmium; it also ameliorated the damaging effects on the neurons morphology and relative distribution of Nissl bodies in the cortical tissue and it is dose dependent.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

The research was carried out in line with humane animal as stated in the guide to care and use in the laboratory by both the National Research Council of Nigeria and Bingham University Ethical Committee guide line.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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