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Evaluation of the Effects of Water Melon Seed Oil (*Citrullus lanatus*) on Cadmium Induced Cerebral Toxicity in Male Wistar Rats.

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ABSTRACT
Cadmium is a toxic heavy metal that accumulates predominantly in soft tissues and as such is currently one of the most important occupational and environmental pollutants. The study evaluated the potential protective effects of watermelon seed oil on cadmium-induced toxicity in the cerebrum of male Wistar rats. Group 1 recieved 2 ml/kg of distilled water. Group 2 received 5 mg /kg bwt of cadmium chloride only. Group 3 received 5 mg /kg bwt of cadmium chloride + 500 mg / kg btw of CLSO as high dose. Group 4 received 5 mg /kg bwt of cadmium chloride + 250 mg / kg btw of CLSO as low dose. Group 5 received 5 mg /kg bwt of cadmium chloride + 10 mg / kg bwt of succimer. The administration was done through oral intubation and lasted 28 days. The experimental animals were observed daily and weighed weekly for physical changes. Neuro- behavioral study on anxiety related behaviors was accessed weekly using elevated plus maze test. On the 29 th day of the experiment, the final body weights were taken and euthanized using 75 mg /kg ketamine IP. The brain tissues were homogenized using 5 times (w/v) homogenizing buffer (pH 7.4). The homogenate was centrifuged at 4000 rpm to get the supernatant for biochemical analysis. While organ/ body weight revealed no significant changes, behavioral study show that *Citrulus lanatus* seed oil significantly ($p<0.05$) increased rearing frequency, grooming frequency and the number of entry into the open arm of the elevated plus maze relative to control. The biochemical assay showed statistically increased mean MDA across the groups when compared with the control ($p <0.001$). Although, there were statistical decrease SOD and GSH of the treated groups ($p <0.001$) when compared with the control, the mean CAT showed no significant difference across the groups in relation to the control. The histology showed that Co-treatment with CLSO prevented the neuronal degenerations of the cerebral cortex when compared with the control. CLSO ameliorated the effects of CdCl2–induced degeneration of cerebral cortex neurons, thus demonstrating its potential to protect cerebral cortex neurons from cadmium toxicity.

Key words: Cadmium chloride. Oxidative stress, Toxicity *Citrulus lanatus*, Histology

INTRODUCTION
Production of peroxides and free radicals as a result of distortion of the normal redox state of cells can lead to damage of all components of the cell in the body.[1] This as a result. caused by imbalance between the systemic expression of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage.[47] The generation of the free radicals are thought to be concerned in the development of several molecular diseases such as cancer, Parkinson`s disease, Alzheimer's disease atherosclerosis, heart failure, myocardial infarction and a host of others.[6,23,24]
Exposure to heavy metals have been implicated to be a major cause of cellular toxicity and as such plays a significant role in the etiology of several disease conditions globally and most especially among developing countries.[23] These target many systems of the body and can cause a multitude of different symptoms.[9,45]

Cadmium is a heavy metal that is incredibly toxic to both humans and animals which has a life-long exposure due to its use in most consumables and essential products.[38,31] These however, includes its use as a coating for iron, steel and copper, stabilizers in rubber and plastics, cigarette papers, fungicides and in many other products in our industries which often contaminate the water ways, air and food.[7] Other sources of cadmium in the environment include anthropogenic activities such as burning of fossil fuels, incineration of municipal waste containing plastics and nickel-cadmium batteries, drug contaminations and agricultural activities.[2,32]

The toxic effects of cadmium has been demonstrated in several organs, it causes tissue injury through creating oxidative stress, epigenetic changes in DNA

expression, inhibition or up regulation of transport pathways in the proximal S1 segment of the kidney tubule.[48,14] Other pathologic mechanisms include competitive interference with the physiologic actions of Zn, Ca and Mg, inhibition of heme synthesis and mutilation of mitochondrial functions through induction of apoptosis, formation of metallothionine and consequent depletion of glutathione which leads to structural distortion of proteins due to cadmium binding to sulfhydryl groups of proteins.[34] Its toxicity contributes to a large number of health conditions such as heart disease, cancer, skeletal dysfunctions, neurodegenerative diseases and diabetes.[8,33]

Acute central and peripheral neurotoxicity of cadmium has been reported in recent studies.[41] Cadmium induces cellular damage and lipid peroxidation in brain.[18] Its effect on monoaminoxidase (MAO) is responsible for oxidative deamination of monoamine neurotransmitters.[27] Cadmium increases production of free radicals in CNS and decreases cellular defense against oxidation.[29,21] In general, the outcomes of this mechanism are olfactory dysfunction, neurobehavioral defects in attention, disorder in psychomotor activity, and memory.[28,43,44] Cadmium poisoning has been reported to cause several neurodegenerative disorders which include Parkinson, Alzheimer, and Huntington's diseases accompanying with loss of memory and behavioral changes.[30,26,4]

Vegetable oils account for 80% of the world's natural oils and fat supply with increasing importance in nutrition owing to their dietary energy, antioxidant and raw materials potentials for industries.[13,19] Growing evidence has suggested that individual fatty acids from seeds may play different roles in human health especially in acute and chronic diseases management.[12] Diets rich in essential specific fatty acid may provide potential prevention of a number of health problems or diseases.[52,34]

However, there has been a global campaign towards the uses of natural phytochemicals present in natural products such as fruits, vegetables and their extracts for the management of various diseases and as useful remedies for the alleviation of human illnesses.[10,25]

Watermelon (*Citrullus lanatus*) is taxonomically classified as a member of the Curcubitaceae family. It is a common fruit in Nigeria; known as Anyu in Igbo, Kankana in Hausa and Elegede in Yoruba.[52] Other members of the family include pumpkins, cucumbers, squash, and other melons. It is a popular fruit in many parts of the world and widely distributed in the tropics that serves as a thirst-quencher owing to its high water content.[5] The fruit comes in various shapes, sizes and rind pattern.[50] Although the seed of watermelon is often discarded as waste, but it content includes various amounts of carbohydrates, phenol, flavonoids, protein, fiber, phosphorus and iron.[53,39] Proximate analysis of the seeds revealed very high fat content (47.9%) followed by protein (27.4%) and carbohydrates (10.0%).[42,40]

MATERIALS AND METHODS

Ethical Approval: Ethical approval for the study was sought from the Ethical Review Committee for Animal Experimentation of Ahmadu Bello University, Zaria, Nigeria with the approval NO;ABUCAUC/2012/087.

Experimental Protocol: Twenty five apparently healthy adult male Wistar rats weighing between 150g to 200g were purchase from the Department of Human Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, Ahmadu Bello University Zaria, Kaduna State, Nigeria. The animals were acclimatized for one week in the animal house of the Department of Human Anatomy. The animals were fed with rat feed and water *ad libitum* throughout the experimental period. The rats were divided into five groups of five rats each.

Chemicals and reagents: 10 g of Cadmium Chloride manufactured by Kermel Chemical Laboratory limited Dagenham China was purchased from Cardinal Science Suppliers store in Zaria, Kaduna state, Nigeria. The reagent was authenticated in the Department of Chemistry, Faculty of Physical Sciences, Ahmadu Bello University, Zaria.90ml of watermelon seed oil manufactured by Hemani international KEPZ Karachi-Pakistan and licensed by Hemani Herbal LLC, 215 Pineda St Unit121, Longwood, FL 32750, USA was purchased from a reputable store in Sabon Gari market, Zaria, Kaduna State. 5g Meso 2, 3-dimercaptosuccinic acid (Succimer, DMSA) was ordered from Sigma-Aldrich Chemical Limited, Germany and was authenticated in the Department of Chemistry, Faculty of Physical Sciences, Ahmadu Bello University, Zaria.10 mg/kg body weight was administered to the animals as standard drug. Growers feed from Vital feed was obtained from Samaru Market Zaria, Kaduna, Nigeria, and was used to feed the animals throughout the experimental period.

Experimental Procedure: The animals were randomly divided into five groups of five animals per group. Group 1 received 2 ml/kg body weight of distilled water, Group 2 received 5 mg /kg body weight of $CdCl_2$ only, Group 3 received 250 mg/kg body weight of WMO as low dose + 5 mg/kg body weight of $CdCl_2$, Group 4 received 500 mg/kg body weight of WMO as high dose + 5 mg/kg body weight of $CdCl_2$,[54] Group 5 received 10 mg/kg body weight of the Succimer + 5 gm/kg body weight of $CdCl_2$. The dosage of the WMO was adopted from work done by,[12] who determined the LD_{50} of WMO to be a value above 5000 mg/kg body weight.

Neurobehavioral Study: All experimental procedures were carried out in a quiet room in the Department of Human Anatomy, Faculty of Basic Medical Sciences, College of Medical Sciences, Ahmadu Bello University, Zaria, Kaduna State, Nigeria.

Elevated plus maze test: The elevated plus maze test was performed according to the method of.[11]The test was employed to study anxiety related behaviors in Wistar rats. The apparatus consisted of two open arms 50 cm by 10 cm and two close arms 50 cm by 10 cm by 40 cm connected through a central platform 10 cm by 10 cm. The arms were arranged in the cross shaped with the open arms facing each other and the closed arms facing each other. The maze was elevated 45 cm above the floor. To begin the testing, the rat were lifted from the home cage at the tail and supported around the neck. The rats were each gently placed at the center of the maze with their faces directed towards the one of the closed arms. The researcher then gently withdrew from the test apparatus and observes the activities of the rats for five minutes within the maze. The general activities of the rats within the maze were observed for 5 minutes. The number of entries into the closed arms and the open arms as well as the duration of permanencies in those areas were observed and recorded in seconds. The number of rearing, grooming and head deep were also recorded. The floor and the walls of the closed and opened arms were cleaned with 70% alcohol after each trail. After each trail, the rats were returned to their cages.

Morphological Studies: All the experimental animals` body weight was taken at the onset of treatment to determine the initial body weight and weekly throughout the study. The animals` body weight was also taken on the last day of administration before sacrifice to determine the final body weight of the animals. The weight changes of the animals in each group were calculated by subtracting the initial body weight from the final body weight. The data obtained were subjected statistical analysis and reported.

Animal Sacrifices: After the last day of administration, the animals were left for 12 hours, fasted overnight the day before they were sacrificed. The animals were euthanized by injecting ketamine intraperitoneally and sacrificed through cardiac puncture, Incision was made through the mid-sagittal suture and their brain removed and weighed. Tissue homogenate was prepared using half of the brain for biochemical assays and the others fixed in Bouin`s fluid for histological analysis. The supernatants were taken to the Histology preparation laboratory of the Department of Human Anatomy Ahmadu Bello University Zaria for tissue processing, estimation of biochemical.

Estimation of Oxidative Parameter: Preparation of homogenate - The brain tissue was homogenized with 5 times (w/v) Sodium phosphate buffer at 50Mm, pH 7.4 plus150 mm KCl and centrifuged at 4000per gram for ten minutes (Centrifuge Hitachi CR21,Hitachinaka,Japan).The supernatant was collected for biochemical analysis in the Department of Pathology, Faculty of Clinical Medical Sciences, Ahmadu Bello Teaching Hospital Samaru Zaria, Nigeria.

Determination of catalase activity using tissue homogenate: Catalase activity was determined using the method described by [46] and the absorbance was read at 570 nm. Standard cure was made by plotting the absorbance obtained at various levels of the assay. The catalase activity was obtained from the graph of the standard curve.

Determination of superoxide dismutase (SOD) Activity using tissue homogenate: Superoxide Dismutase (SOD) activity was determined by a method described by.[20] Absorbance was measured every 30 seconds up for a total of 150 seconds at 480 nm from where the SOD activity was calculated.

Assessment of lipid peroxidation using tissue homogenate: Lipid peroxidation as evidenced by the formation of TBARS was measured by the method of [36] The absorbance of the pink supernatant was measured against a reference blank using a spectrophotometer at 535nm.

Assay of reduced glutathione using tissue homogenate: Concentration Reduced glutathione (GSH) concentration measurements will be done according to the method of.[15] The absorbance was read at 412 nm.

Data analyses: Results were analyzed using the statistical package for social scientist (SPSS version 18). Data were reported as mean±standard error of mean (SEM). One way analysis of variance (ANOVA) was used to compare the means differences between and within the groups, with values of $p<0.05$ considered to be statistically significant. Turkey's LSD post hoc test was also done to test for the least significant difference within the experimental groups. Results were presented in graphs and tables were appropriate.

RESULT

Physical Observation and Weight changes: Showed that the animals in Group 1 (Control) were very active with no physical observable changes throughout the administration. Although, the treated groups showed several level of decreased physical activities, gnawing and restlessness. Scratching of the mouth, nostril and frequent urination during the first 14 days of the administration. However, the animal in the treated groups showed significant increase in physical activities during the last 14 days of the administration.

There were no significant difference in the body weights and the brain weight ratios as shown in Table 1. Although, animals in Group 1 and 5 showed increased mean body weight when compared with the treated groups. The animals in Group 2 and Group 4 showed a drastic decline in the mean body weight when compared with the control. However, there were no observable changes in the mean body weight of animals in Group 3 when compared with the control as shown in Table 1.

Table 1: Effects of water melon seed oil and cadmium chloride on weight Changes

Groups	Initial	Final	WD	Brain	Cere	Celle
1	178.00±17.65	194.25±21.31	16.25±4.52	1.70±0.04	0.47±0.03	1.22±0.02
2	180.25±15.89	175.50±16.32	-4.75±1.44	1.70±0.05	0.41±0.04	1.29±0.02
3	179.20±6.89	179.80±10.79	0.20±6.81	1.66±0.03	0.42±0.02	1.22±0.03
4	177.00±10.07	173.80±4.31	-2.00±6.25	1.71±0.05	0.48±0.01	1.22±0.04
5	168.75±12.49	182.25±6.66	13.50±7.14	1.65±0.05	0.43±0.02	1.26±0.05
P	0.971	0.812	0.082	0.809	0.257	0.522

Group 1= Distilled water (H_2O). Group 2 = 5 mg /kg bwt $CdCl_2$only. Group 3 = 5 mg /kg bwt $CdCl_2$500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$250 mg / kg bwt CLSO. Group5 = 5 mg /kg bwt $CdCl_2$+ 10 mg /kg bwt of Succimer.wd;Weight difference.Cere; Cerebrum. Celle;Cerebellum.

Behavioural Test Evaluation: The test for the elevated plus maze carried out on the experimented animals showed that the animals in GROUP 2 had the least number of entries into the open arms and recorded the highest percentage of permanence in the closed arm with least rearing and grooming frequency. The animals in GROUP 3, GROUP 4 and GROUP 5 which served for the treated groups showed improved level of head dip and rearing frequencies, increased number of entries into the open arm, increased percentage duration in the open arm and decreased percentage duration in the closed arm when compared with the control as shown in Table 2.

Table 2: Effect of cadmium chloride exposure and treatment with water melon seed oil on anxiety related behaviors using Elevated plus maze test.

Groups	NEOA	NECA	RF	GF	HD	DOA	DCA
1	2.25±0.08	3.00±0.21	9.00±0.78	6.75±0.25	2.25±0.11	19.00±2.01	81.00±6.01
2	0.25±0.05	2.25±0.18	7.00±0.41	4.75±0.75	3.00±0.91	1.00±0.01	99.00±4.00
3	2.00±0.05	1.00±0.00	4.60±0.56	3.20±0.58	0.20±0.01	14.80±3.92	85.20±7.92
4	1.00±0.05	2.40±0.17	7.60±0.63	3.80±0.16	3.40±1.23	10.40±1.59	89.60±4.59
5	1.75±0.05	2.00±0.11	5.75±0.11	3.00±0.82	1.75±1.18	18.00±3.69	82.00±7.69
p	0.279	0.216	0.377	0.085	0.293	0.309	0.309

Group 1= Distilled water (H_2O). Group 2 = 5 mg/kg bwt $CdCl_2$only. Group 3 = 5 mg /kg bwt $CdCl_2$500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$250 mg / kg bwt CLSO. Group5 = 5 mg/kg bwt $CdCl_2$+ 10 mg /kg bwt of Succimer.NEOA;Number of entry into open arm,NECA;Number of entry into closed arm,RF; Rearing frequency, GF;Grooming,HD;Head dip, DOA;Duration in the open arm, DCA; Duration in the closed arm.

Biochemical Studies: The biochemical assay showed statistically increased mean MDA across the groups when compared with the control ($p < 0.001$).However, group 2 recorded the highest mean MDA while group 5 had the lowest mean MDA when compared with group 3 and group 4. The mean CAT showed statistically significant decrease across the groups when compared with the control ($p<0.048$).However, there was increase mean CAT of Group 4 animals when compared with Groups 3 and 5. However, there were significant difference in the mean SOD of group 4 when compared with other groups ($P < 0.003$). In addition, significant differences were obtained in the mean GSH of Groups 2 when compared with other groups ($P < 0.001$).However significant differences were obtained between group 4 when compared with the control group and group 2 while there were significant difference between group 5 when compared with groups 2 and 3 as shown in FIG, 1,2,3 and 4.

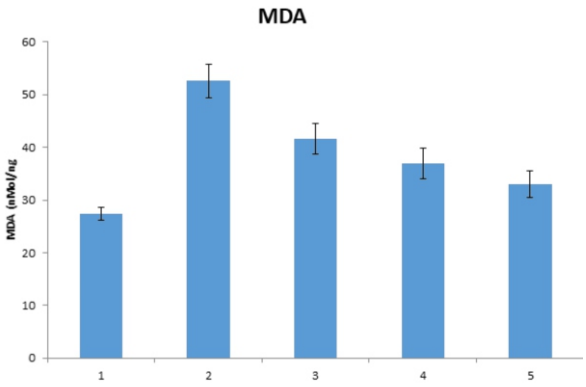
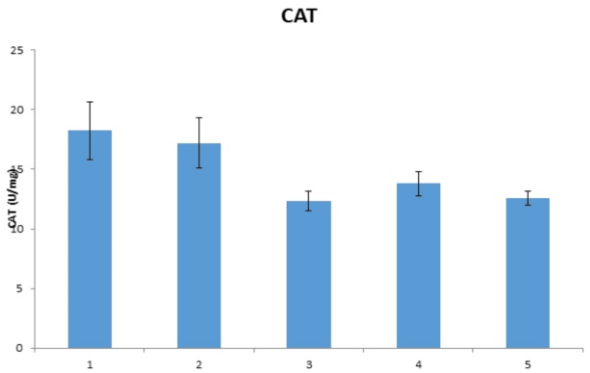
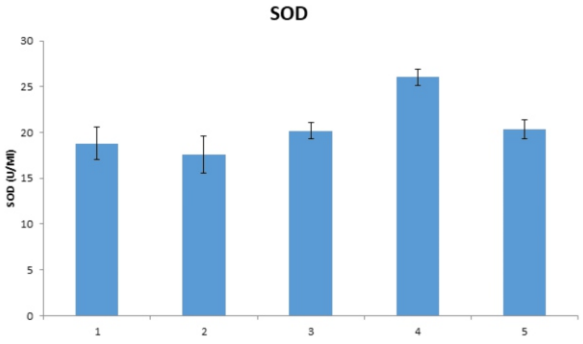


Figure1: MDA concentration in the brain tissue of animals exposed to cadmium chloride
Group 1= Distilled water (H_2O). Group 2 = 5 mg /kg bwt $CdCl_2$ only. Group 3 = 5 mg /kg bwt $CdCl_2$ 500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$ 250 mg / kg bwt CLSO. Group5 = 5 mg /kg bwt $CdCl_2$ + 10 mg /kg bwt of Succimer.



Figur 2: CAT concentration in the brain tissue of animals exposed to cadmium chloride
Group 1= Distilled water (H_2O). Group 2 = 5 mg /kg bwt $CdCl_2$ only. Group 3 = 5 mg /kg bwt $CdCl_2$ 500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$ 250 mg / kg bwt CLSO. Group5 = 5 mg /kg bwt $CdCl_2$ + 10 mg /kg bwt of Succimer.



Figur3: SOD concentration in the brain tissue of animals exposed to cadmium chloride
Group 1= Distilled water (H_2O). Group 2 = 5 mg /kg bwt $CdCl_2$ only. Group 3 = 5 mg /kg bwt $CdCl_2$ 500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$ 250 mg / kg bwt CLSO. Group5 = 5 mg /kg bwt $CdCl_2$ + 10 mg /kg bwt of Succimer.

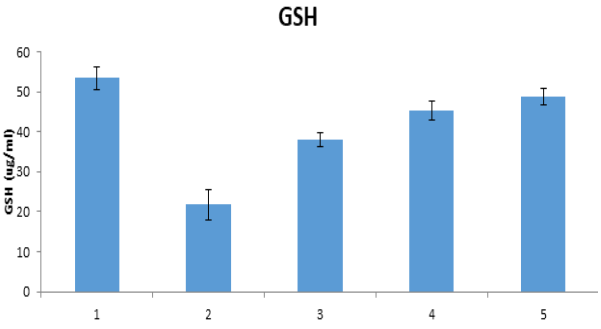


Figure4: GSH concentration in the brain tissue of animals exposed to cadmium chloride
Group 1= Distilled water (H_2O). Group 2 = 5 mg /kg bwt $CdCl_2$ only. Group 3 = 5 mg /kg bwt $CdCl_2$ 500 mg /kg bwt CLSO. Group 4 = 5 mg /kg bwt $CdCl_2$ 250 mg / kg bwt CLSO. Group5 = 5 mg /kg bwt $CdCl_2$ + 10 mg /kg bwt of Succimer.

Histological Studies: The cyto-architectural micrographic observations showed cellular changes in the tissue studied. GROUP 1 which served as the control had normal cytoachitectural presentation of the cerebral cortex; the neurons were arranged into six layers with each differing in cellular morphology, size and density. The internal pyramidal layer (layer V) showed large pyramidal cells often called ganglions or Betz cells of the motor cortex as shown in plate 1.While the treated groups showed different levels of neuronal degenerative changes and vacuolated cell bodies as shown in Plate2, Plate 3, Plate 4 and Plate 5.

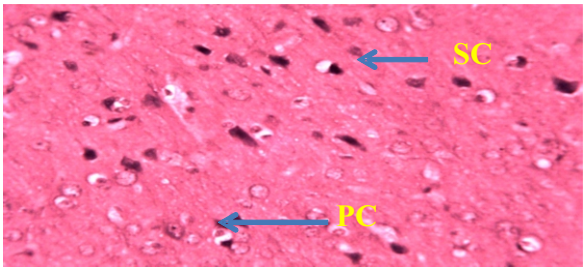


Plate 1: Section of the layer five of cerebral cortex of Wistar rat in group 1 (Control) showing normal Pyramidal cells and Stallet cells (H and E X 250).

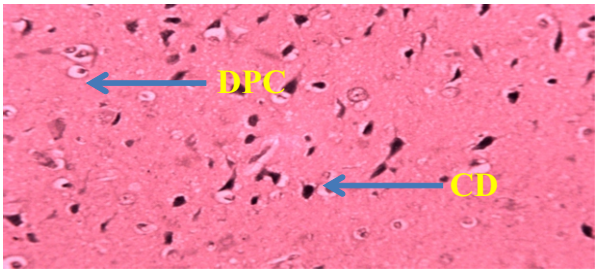


Plate 2: Section of the layer five of cerebral cortex of Wistar rat in group 2 (Toxic group) showing disintegrated Pyramidal cells,DPC; Cellular degeneration,CD. (H and E X 250).

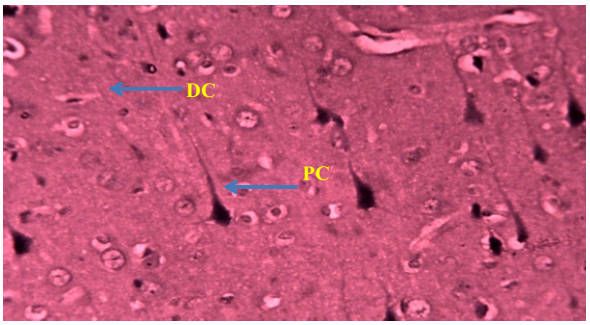


Plate 3: Section of the layer five of cerebral cortex of Wistar rat in group 3, showing Pyramidal cells,PC; degenerating cells, DC. (H and E X 250).

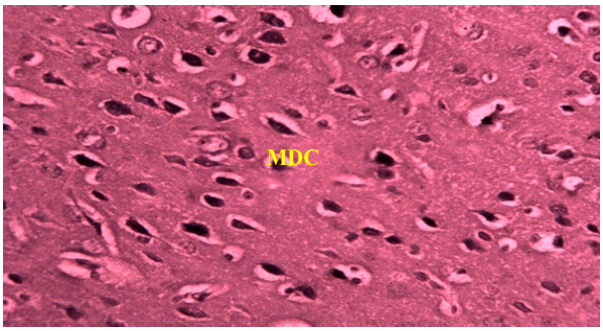


Plate 4: Section of the layer five of cerebral cortex of Wistar rat in group 4, showing Mild Degenerating cells, DC. (H and E X 250).

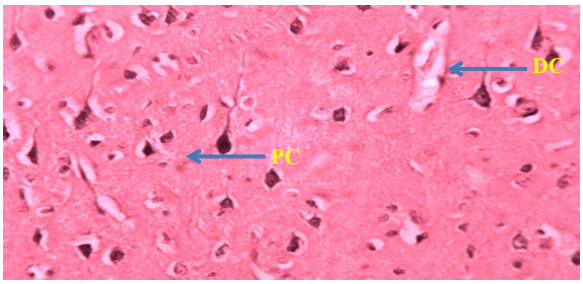


Plate 5: Section of the layer five of cerebral cortex of Wistar rat in group 5, showing Pyramidal cells,PC; Degenerating cells, DC. (H and E X 250).

DISCUSSION

Disruptions in physical, social, emotional and cognitive behavior are common in neurodegenerative disease and in many forms of psychopathological dysfunctions.[1,35] The animals in Group 1 (Control) and Group 5 were very active with no physical observable changes throughout the administration. Although, the animals in the treated groups showed decreased physical activities such as Gnawing and restlessness, scratching of the mouth, nostril and frequent urination. These changes could be linked to the effects of cadmium that might have caused behavioral changes in the animals. Cadmium toxicity has been reported to disturb brain chemistry leading to depression, anxiety, and weakened immunity.[17] Cadmium disturbs the neurotransmitter dopamine, resulting in low energy, lack of motivation, and depression.[54] [51] reported that cadmium poisoning through diet and environment cause severe symptoms such as anxiety, irritability, mood changes and depression. However , the animals in groups 3 as well as those in groups 4 and 5 showed significant increase in physical activities during the administration which could be attributed to the ameliorative effects of Water melon seed oil and Succimer. This findings, however, is in agreement with the result of.[37]

Treatment with CLSO improved rearing frequency (RF), grooming frequency (GF), and number the of head dip (NHD). In addition, the mean percentage occupancy of the open arm all of which suggested

improved locomotive, exploratory and reduced anxiolytic behaviors when compared with the control. Similarly, succimer gave comparable effects with the CLSO by improving all these parameters. However, the rats that received $CdCl_2$ only recorded decreased RF, GF, NHD and increased mean percentage occupancy of the closed arm all of which suggested anxiolytic behaviors. This result is in agreement with the work of .[41]

Although. Increased mean body weight were observed in the control group and in the groups treated with CLSO and succimer than those treated with $CdCl_2$ only. However. these changes were not significant. This suggests that despite the toxicity of $CdCl_2$, it did not cause sufficient organ or tissue necrosis which might have led to significant decrease in the present study. This finding is in agreement with the work of.[3,14] In addition, the absence of a significant increase or decrease in the relative brain body weight ratio across the groups suggested the absence of significant tissue inflammation among the surviving rats or possession of anti-inflammatory potentials of CLSO which agreed with the findings of.[4,41]

Oxidative stress is a common mediator in pathogenicity of established neuro- pathological risk factors. It contribute to residual risk resulting to Functional oxidative modifications of cellular proteins, both reversible and irreversible which are a causal step in cellular dysfunctions.[51]The present study showed a significant increase in the mean MDA ($P < 0.05$) of the rats in group 2 when compared with the control. In addition, a significant decrease in the mean CAT, SOD and GSH ($P < 0.05$) were equally observed in the groups when compared with the control. However, a significant increase in the mean CAT, SOD and GSH ($P < 0.05$) were observed in groups 3, 4 and 5 when compared with group 2. This could be attributed to the ameliorative effects of water melon seed oil which contains Lycopene and Flaviniods that have been reported to have anti-oxidant properties. This finding is however in agreement with the results of .[17,4]

The cyto-architecture of the cerebral cortex of animals in the control group were normal showing cortical neurons with distinct cellular outlines, large soma with large nuclei showing visible nucleoli as shown in Pate 1. This result is similar to the work of.[41] However, the histology of the cerebral cortex of the animals treated with CdCl2 demonstrated evidence of toxicity as shown by degenerating neurons Plate 2. Some of these neurons were pyknotic while others involved several levels of cellular aggregations and disintegration which were evidences of onset of neuronal degeneration. The neuronal degeneration induced by $CdCl_2$ is in agreement with the published reports that the brain is often affected by cadmium intoxication.[51,4] The vulnerability of the central nervous (CNS) to cadmium chloride toxicity has been attributed to varying factors like oxidative stress due to free radical generation, neurotransmitter disruption and stimulation of the neural excitoxins, resulting in damage to many parts of the brain, its influence on DNA repair mechanisms and direct interaction with DNA molecules all of which may lead to genotoxicity.[51] The ability of cadmium chloride to cause membrane porosity and in turn accumulate in the brain at much higher concentrations also promotes neurotoxicity.[4] The consequence of degeneration of cortical neurons will include the inability of the animal or human to perform executive functions such as self-control, planning, reasoning, attention, decision making, judgments, overall control of abstract thoughts.[49,22,41]

In rats, the acute implication would include decreased exploratory activities strengthened by our findings. There could also be upper motor neuron lesion manifestations since the corticospinal tract and some other important corticofugal projection fibers are associated with the cortical neurons,[25,41] however, not demonstrated these in these research findings. The cortical micrographs of CLSO and succimer treated groups showed mild neuronal degenerations relative to the toxic group ($CdCl_2$) as shown in Plates 3,4 and 5 is an evidence that CLSO ameliorated the damaging effects of CaCl2. This finding is supported by the fact that substances with antioxidant capabilities can neutralize or reduce the oxidative damage of the toxic effects of $CdCl_2$.[4,37]

In conclusion, the various observations from the present study, however, justify some deleterious consequences of cadmium exposure which may lead to histo- pathological changes, oxidative stress, anxiety related behaviours. *Citrulus lanatus* seed oil contains lycopene, Flavinoids and other important phytochemicals which have been proven as strong antioxidants. Hence, potentiates ameliorative effects against cadmium induced neurotoxicity. Consumption of water melon seed oil should be encouraged in a dose dependent most especially by urban residencies and individuals that are occupationally exposed. It should be used as ointment for body massage as well as major ingredients in cosmetic products.

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