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Effects of Launaea taraxacifolia (Wild Lettuce) Aqueous Extract in Cadmium Chloride-Induced Alzheimer's Disease-Like Neurodegeneration in Male Wistar Rats

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Abstract- Alzheimer's disease (AD), characterized by progressive neurodegeneration and cognitive dysfunction, continues to pose significant treatment hurdles, particularly when environmental neurotoxins like cadmium trigger or exacerbate the condition. Launaea taraxacifolia, a medicinal plant with known antioxidant property, may offer therapeutic potential against cadmium chloride-induced Alzheimer's disease-like neurodegeneration. This study was designed to investigate the efficacy of Launaea taraxacifolia aqueous extract in mitigating cadmium chloride-induced Alzheimer's disease-like neurodegeneration in male wistar rats. This study used thirty-two (32) adult male wistar rats. There were four groups of eight rats each. For 21 days, Group I were given distilled water orally; Group II were given 5 mg/kg of CdCl2 orally; Group III were given 400 mg/kg of LTAE orally; and Group IV were given 5 mg/kg of CdCl2, followed by 400 mg/kg of LTAE orally. CdCl2 caused a significant decrease (p<0.05) in neurobehavioural parameters (Y maze and open field), revealed alteration of the neuronal cytoarchitecture (neuronal loss and neurofibrillary tangles) of the cerebral cortex and hippocampus, respectively. Similarly, co-administration of LTAE with CdCl2 inhibited cadmium chloride-induced Alzheimer's disease-like neurodegeneration by reversing the altered microanatomy of the cerebral and hippocampus of rat, and changes in neurobehavioural parameters. It is concluded that LTAE effectively ameliorates Alzheimer's disease-like neurodegeneration following CdCl2 treatment and maybe a therapeutic strategy against the neurological consequences of CdCl2 overexposure.

Keywords: Alzheimer's disease, Cadmium Chloride, Neurodegeneration, Launaea taraxacifolia, Cresyl fast violet staining.

I. INTRODUCTION

With millions of cases worldwide, Alzheimer's disease (AD), a progressive degeneration of neurons, mainly in the cortical and hippocampus regions, is the most common type of dementia and a rising public health concern (Priyanka *et al.,* 2025). It is a neurodegenerative illness that is linked to cognitive decline, memory loss, and behavioral abnormalities (Xiqi *et al.,* 2025). Emerging research shows that environmental pollutants play a significant role in the development and progression of AD, even though genetic predisposition and aging remain the main risk factors (Mertaş and Boşgelmez, 2025). Among these, the hazardous heavy metal cadmium (Cd) has drawn more attention due to its potential for neurotoxicity.

Industrial processes, battery manufacturing, cigarette smoke, and tainted water or food sources are the main causes of cadmium's widespread presence in the environment (Zaman *et al.,* 2022). Cadmium chloride ($CdCl_2$) serves as a chemical compound that readily dissolves in water, allowing cadmium ions (Cd^{2+}) to be easily absorbed by biological tissues. Cadmium builds up in the body after absorption, including the central nervous system, where it remains for many years (Qu and Zheng, 2024). The pathophysiology of Alzheimer's disease is linked to oxidative stress, mitochondrial dysfunction, and chronic neuroinflammation, all of which are caused by cadmium's ability to cross the blood–brain barrier (Qing *et al.,* 2024).

According to experimental research, cadmium exposure can mimic important aspects of AD by causing hippocampus damage, compromising synaptic function, and interfering with learning and memory.

The two main pathological features of AD, tau protein hyperphosphorylation and amyloid beta accumulation, have also been demonstrated to be facilitated by cadmium (Babic *et al.,* 2023). Cadmium also causes neuronal death by activating apoptotic pathways, which include upregulating pro-apoptotic proteins (Wen *et al.,* 2021).

In areas where environmental cadmium levels are high, it is crucial for public health to comprehend the mechanism underlying the association between cadmium exposure and Alzheimer-like neurodegeneration. One promising avenue for minimizing cadmium-induced neurodegeneration and lowering the risk of Alzheimer's disease is the investigation of potential protective agents, such as antioxidants derived from plants.

The leafy green vegetable and medicinal plant *Launaea taraxacifolia*, also referred to as African lettuce, is found throughout West Africa, especially in Nigeria, Ghana, and the neighbouring countries (Bello *et al.,* 2018). It has long been a staple of the local diet and has been used in folk medicine to treat a number of conditions, such as inflammation, fever, high blood pressure, and liver problems (Koukoui *et al.,* 2021; Obazelu and Faluyi, 2023).

According to studies on phytochemistry, L. Flavonoids, phenolics, saponins, alkaloids, and vitamins A and C are among the many bioactive substances found in taraxacifolia that have strong anti-inflammatory, cytoprotective, and antioxidant effects (Anyanwu *et al.,* 2022). A major pathway linked to neurodegeneration and heavy metal toxicity, oxidative stress, is reduced and reactive oxygen species (ROS) are neutralized by these constituents (Adinortey *et al.,* 2018).

Launaea taraxacifolia may have neuroprotective effects because of its capacity to scavenge free radicals, regulate inflammatory pathways, stabilize neuronal membranes, and prevent apoptosis. In conditions involving neurotoxicity and cognitive decline, such as cadmium-induced neurodegeneration, *Launaea taraxacifolia* is being studied as a possible therapeutic agent due to its traditional use and increasing experimental support. In this case, it might provide an inexpensive, natural way to lessen neurological damage caused by environmental toxins. This study aims to investigate the potential protective effects of *Launaea taraxacifolia* aqueous extract in cadmium chloride-induced Alzheimer's disease-like neurodegeneration in male Wistar rats.

II. MATERIALS AND METHODOLOGY

A. Ethical Approval

All procedures were in accordance with the National Institute of Health Guidelines for the Care and Use of Laboratory Animals. Ethical approval was obtained from Centre for Research and Development, Federal University of Technology Akure, with ethical number: (FUTA/ETH/25/235).

B. Preparation of Launaea taraxacifolia Aqueous Extract

Fresh leaves of *Launaea taraxacifolia* were collected, air-dried for four days, and then ground into a fine powder. Aqueous extraction was done by the method of Owoeye et al. (2015).

C. Experimental Animals

Thirty-two (32) adult male Wistar rats weighing 200–250 ± 15 g were used for this study. At the ideal temperature and with a 12-hour light/dark cycle, the rats were housed in ventilated cages. For the duration of the experiment, the animals were given water at will and fed a typical laboratory animal diet. Prior to the start of administration, the rats were acclimatized for fourteen days. Following the National Institute of Health Guidelines for the Care and Use of Laboratory Animals, 2008, all of the animals used in the experiment were treated in compliance with the rules governing animal research.

D. Experimental Design

The thirty-two (32) Wistar rats were divided into four (4) different groups with eight rats in each group to ensure even distribution of mean body weight across groups. Every three days, the body weight and average body weight of each group were measured and documented. The animals were treated as follows:

Group I received distilled water orally for 21 days.

Group II received 5 mg/kg $CdCl_2$ orally for 21 days.
Group III received 400 mg/kg LTAE orally for 21 days.
Group IV received 5 mg/kg $CdCl_2$, followed immediately by 400 mg/kg LTAE orally for 21 days.

The treated animal groups were given cadmium chloride ($CdCl_2$) dissolved in distilled water orally via an oral cannula at a dose of 5 mg/kg. The control groups were given the same amount of distilled water under the same circumstances. 400 mg/kg of LTAE was dissolved in distilled water and given orally via cannula every day for three weeks.

E. Neurobehavioural Assessment

Between 10 am and 3 pm, behavioural studies were conducted in a quiet room one hour after the last administration. Before testing a new animal, the equipment was cleaned with 5% ethanol to remove any potential bias brought on by the smells of the previous animal. The tests were recorded using a digital camera and later scored by trained blind observers.

F. Assessment of Cognitive Performance

Cognitive performance was evaluated and performed on the Y-maze as previously described (Akingbade *et al*., 2022). Spontaneous alternation behavior which was scored on Y-maze task assesses short-term spatial memory as a measure of cognitive functions. The apparatus was made of wood, having three arms in shape of a Y. Each arm was 40cm long, 30cm high and 10cm wide. The rats were placed in the Y-maze, at the end of a pre-determined start arm and allowed to move freely for 5min. Arm entry is defined as when the hind paws of the rats are completely within the arm. Spontaneous alternation is defined as rats entering all three arms in the overlapping triplet sets. The percentage of spontaneous alternation was calculated as [spontaneous alternation/ (total number of arm entries – 2)] × 100.

G. Assessment of Gross Behavioural Activity

Locomotor activity was evaluated in an open-field apparatus. Animals were individually placed at the centre of the apparatus (60cm x 90cm x 30cm, divided into six equal squares). Spontaneous ambulation (number of segments crossed with the four paws), number of rearing, and number of centre square entries was recorded for five minutes (Marreilha dos Santos *et al*., 2011).

H. Animal Sacrifice

On the day following the behavioural assessments (22nd day), the rats were euthanized via cervical dislocation and the brains were excised. The brains were immersed in 10% neutral buffered formalin and used for histochemical analysis.

I. Histochemical Analysis

After fixation, the cerebral cortex and hippocampus were excised and processed for routine tissue processing. Cresyl fast violet staining was done by the method of Shafri et al. (2012) for demonstration of neurons and nissl bodies, and bielschowsky staining was done by the method of Lazarus et al. (2018) for the visualization of nerve fibres, axons, neurofibrils and senile plaque. Stained sections were observed under a light microscope.

J. Statistical Analysis

Statistical evaluation was performed using one-way ANOVA followed by Tukey post hoc test using GraphPad Prism 8.0. All values were expressed as mean ± standard error of mean (SEM). A P-value <0.05 was considered significant.

III. RESULTS

A. Effect of LTAE on Neurobehavioural Analysis in $CdCl_2$-induced Neurotoxicity

Figure 1-4 show the effects of LTAE on percentage of spontaneous alternation, spontaneous activity for ambulation and anxiety-like behaviour in Wistar rats across groups. There was a significant decrease ($p < 0.05$) in the percentage of spontaneous alternation, spontaneous activity for ambulation, number of rearing and number of center square entries in animals treated with $CdCl_2$ compared with controls. In addition, rats that received $CdCl_2$ + LTAE and LTAE only showed a significant increase ($p < 0.05$) in the percentage of spontaneous alternation, spontaneous activity for ambulation, number of rearing and number of center square entries as compared with $CdCl_2$ group ($p < 0.05$).

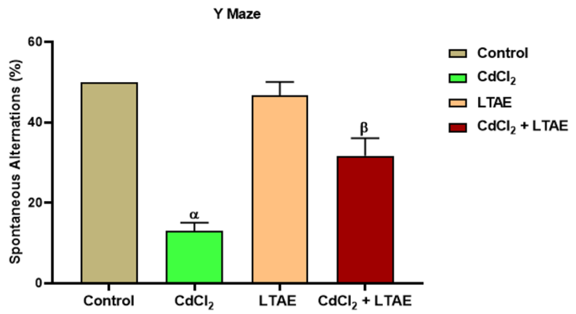


Figure 1: Effect of LTAE on the percentage of spontaneous alternation in $CdCl_2$-induced Wistar rats. All data were estimated with the help of one-way ANOVA trailed by Tukey's multiple comparisons tests. Data were expressed as mean ± S.E.M (n =5). α: significant change with respect to control; β: significant change with respect to $CdCl_2$. Value of $p < 0.05$ was considered significant.

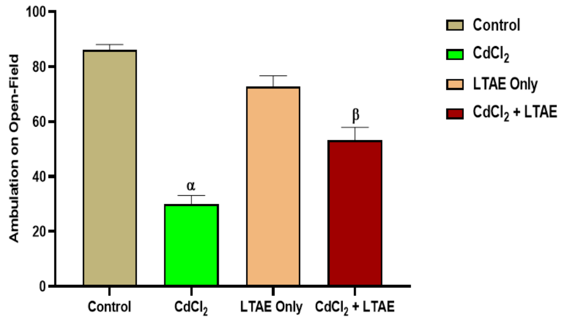


Figure 2: Effect of LTAE on ambulation on open field in $CdCl_2$-induced Wistar rats. All data were estimated with the help of one-way ANOVA trailed by Tukey's multiple comparisons tests. Data were expressed as mean ± S.E.M (n =5). α: significant change with respect to control; β: significant change with respect to $CdCl_2$. Value of $p < 0.05$ was considered significant.

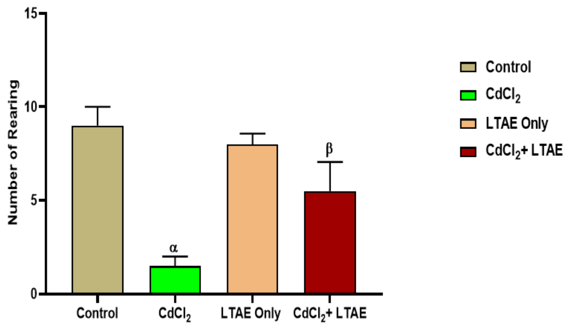


Figure 3: Effect of LTAE on the number of rearing in $CdCl_2$-induced Wistar rats. All data were estimated with the help of one-way ANOVA trailed by Tukey's multiple comparisons tests. Data were expressed as mean ± S.E.M (n =5). α: significant change with respect to control; β: significant change with respect to $CdCl_2$. Value of $p < 0.05$ was considered significant.

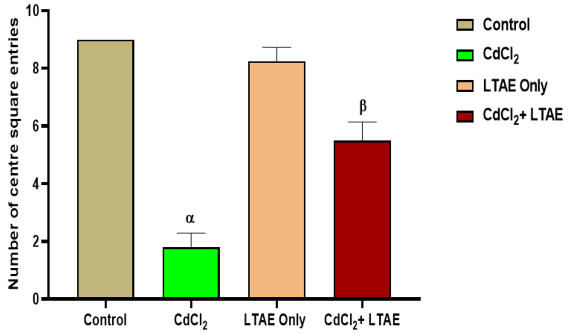


Figure 4: Effect of LTAE on the number of center square entries in $CdCl_2$-induced Wistar rats. All data were estimated with the help of one-way ANOVA trailed by Tukey's multiple comparisons tests. Data were expressed as mean ± S.E.M (n =5). α: significant change with respect to control; β: significant change with respect to $CdCl_2$. Value of $p < 0.05$ was considered significant.

B. *Effects of LTAE on Cresyl Fast Violet Staining of the Brains of Wistar Rats*

Plate 1 – 2 represent the photomicrographs of Cresyl fast violet (CFV) staining of the Cerebral cortex and Hippocampus of Wistar rats across groups. Microscopic examination of the control and the LTAE-alone treated group shows normal basic histochemical features of the cerebral cortex and hippocampus. The histochemical presentations of these groups were dominated by distinct cellular morphology with highly chromatogenic cells. However, the cadmium group ($CdCl_2$), shows degenerated neuronal cells such as chromatolysis and karyolysis. The neuronal cells were however preserved in the cadmium treated groups ($CdCl_2$+LTAE), with improved chromatogenic properties with reduced karyolysis and chromatolysis.

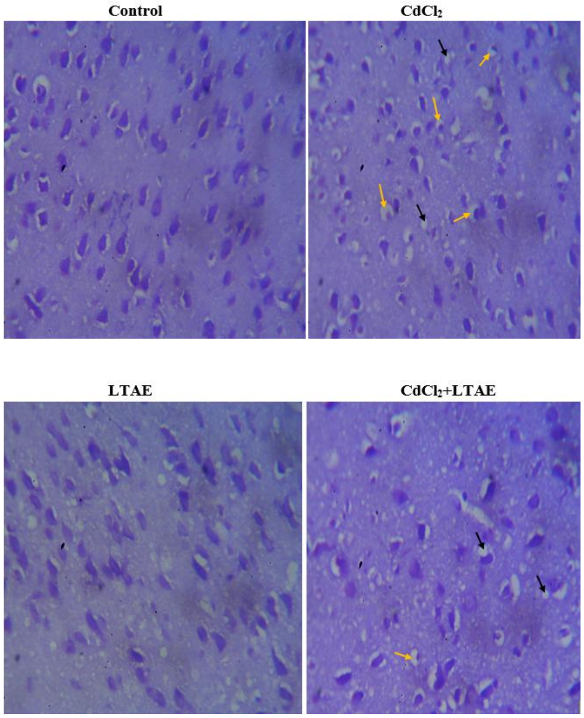
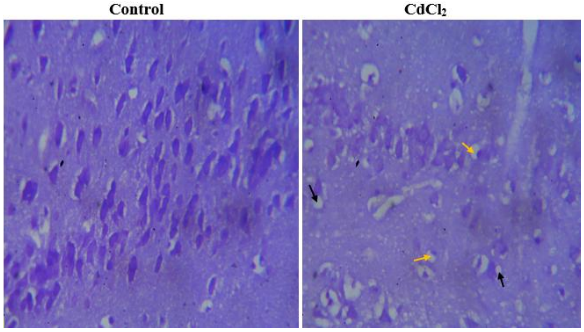


Plate 1: Effects of LTAE on $CdCl_2$-induced histochemical changes in the pyramidal layer of the cerebral cortex of Wistar rats (CFV, 400X). The cerebral cortex of the control group showing highly chromatogenic pyramidal cells with normal neuronal morphology, the $CdCl_2$ group showing degenerated neuronal cells such as chromatolysis (yellow arrows) and karyolysis (black arrows). LTAE alone treated group with highly chromatogenic pyramidal cells, treatment of $CdCl_2$ rats with LTAE shows improved chromatogenic properties of the neuronal cells with reduced karyolysis and chromatolysis. ($CdCl_2$= Cadmium chloride; LTAE= *Launaea taraxacifolia* aqueous extract).



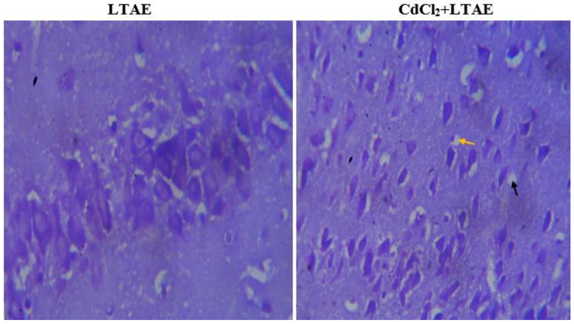


Plate 2: Effects of LTAE on $CdCl_2$-induced histochemical changes in the CA1 region of the hippocampus of Wistar rats (CFV, 400X). The CA1 region of the control group showing highly chromatogenic pyramidal cells with normal neuronal morphology, the $CdCl_2$ group showing reduced staining intensity with degenerated neuronal cells such as karyolysis (black arrows) and chromatolysis (yellow arrows). LTAE alone treated group with highly chromatogenic pyramidal cells, treatment of $CdCl_2$ rats with LTAE shows improved chromatogenic properties of the neuronal cells with reduced karyolysis and chromatolysis. ($CdCl_2$= Cadmium chloride; LTAE= *Launaea taraxacifolia* aqueous extract).

C. Effects of LTAE on Bielshowscky Staining of the Brains of Wistar Rats

Plate 3 – 4 is the photomicrographs of the Bielshowscky staining of the cerebral cortex and hippocampus of wistar rats across groups. Microscopic examination of the control and the LTAE-alone treated group shows normal dark yellow to brown stained cells against yellow background in all brain regions. However, the cadmium group ($CdCl_2$) shows degenerative changes such as neurofibrillary tangles compared to the control group. The neuronal cells were however preserved in the cadmium treated groups ($CdCl_2$+LTAE) with a reduced neurofibrillary tangles compared with the $CdCl_2$ group.

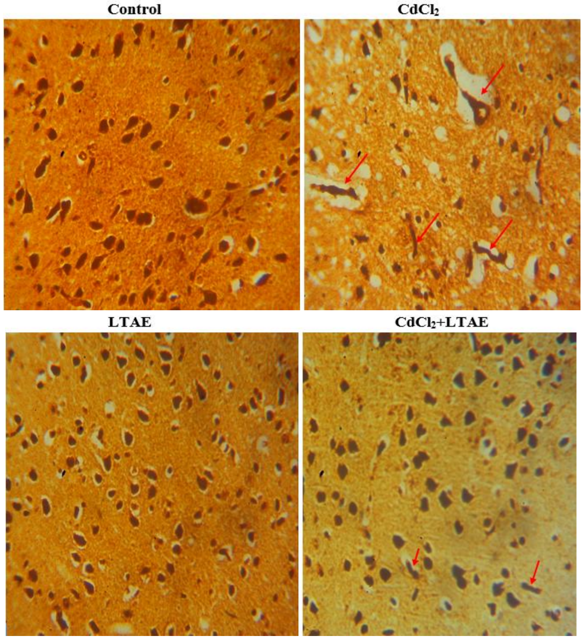
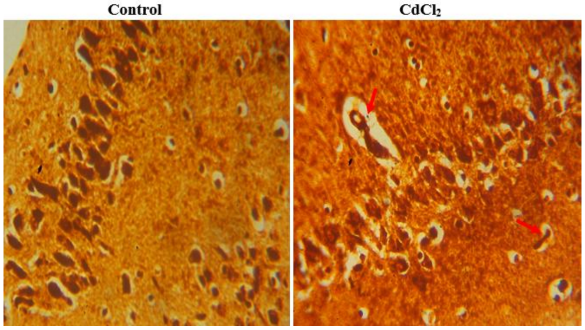


Plate 3: Effects of LTAE on $CdCl_2$-induced histochemical changes in the pyramidal layer of the cerebral cortex of Wistar rats (Bielshowscky, 400X). The cerebral cortex of the control group presents normally stained brown neurons against yellow background. The $CdCl_2$ group was characterised with neurofibrillary tangles (red arrows). LTAE alone treated group with normally stained brown neurons. Treatment of $CdCl_2$ rats with LTAE shows reduced neurofibrillary tangles (red arrows). ($CdCl_2$=Cadmium chloride; LTAE = *Launaea taraxacifolia* aqueous extract).



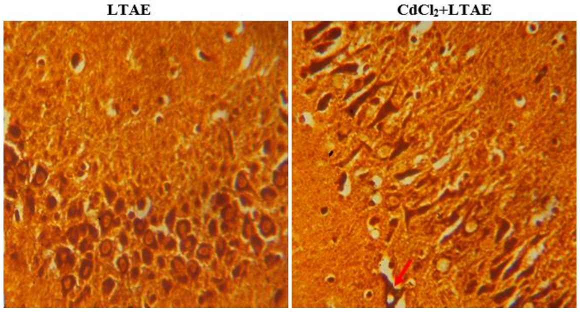


Plate 4: Effects of LTAE on $CdCl_2$-induced histochemical changes in the CA1 region of the hippocampus of Wistar rats (Bielshowscky, 400X). The CA1 region of the control group presents normally stained brown neurons against yellow background. The $CdCl_2$ group was characterised with neurofibrillary tangles (red arrows). LTAE alone treated group with normally stained brown neurons. Treatment of $CdCl_2$ rats with LTAE shows reduced neurofibrillary tangles. ($CdCl_2$=Cadmium chloride; LTAE = *Launaea taraxacifolia* aqueous extract).

IV. DISCUSSION

The results of this study demonstrate that *Launaea taraxacifolia* aqueous extract has a significant protective effect against cadmium chloride-induced Alzheimer's disease-like neurodegeneration in adult male wistar rats. This study is significant due to the increasing prevalence of neurodegenerative disorders like AD and the growing concern about environmental toxicants, such as cadmium, that can trigger or exacerbate such conditions. In the nervous system, cadmium, a highly toxic heavy metal, is known to cause a variety of pathological alterations, mostly by causing inflammation, mitochondrial dysfunction, oxidative stress, disruption of neuronal function and neuronal apoptosis, all of which are key features of AD pathology (Ojo *et al.,* 2023). According to the findings of this study, *Launaea taraxacifolia* can effectively counteract these negative effects and has promising therapeutic potential for reducing cadmium chloride-induced neurodegeneration because of its diverse phytochemical constituents such as flavonoids, phenolics, and vitamins.

The Y-maze test is commonly used to assess working memory and spatial learning abilities. Spontaneous alternation behaviour is a reliable indicator of cognitive function, where a higher percentage of alternations suggests better memory and decision-making ability. However, in this study, there was a significant reduction in the spontaneous alternation behaviour in the cadmium group, indicating cognitive impairment, mirroring early symptoms of Alzheimer's disease. This is in line with the study of Adaze and Gabriel (2022) whereby a significant decrease in spontaneous alternation behaviour in cadmium-treated rats was reported. However, rats treated with *Launaea taraxacifolia* aqueous extract showed a significant improvement in spontaneous alternation percentages, suggesting enhanced memory performance. This study is in agreement with a study conducted by Oluwole et al. (2023) whereby a significant increase in spontaneous alternation in rats that received *Launaea taraxacifolia* aqueous extract as co-treatment with lead was reported. The enhancement in cognition may be due to the antioxidant and anti-inflammatory constituents of the plant, which play a role in modulating brain regions associated with memory (Owoeye *et al.,* 2015). The open field test is commonly used to assess general locomotor activity and anxiety-like behaviour. In this study, cadmium exposure led to reduced locomotor activity, as shown by decreased line crossings and rearing, and increased anxiety-like behaviours, as shown by reduced center square entries in cadmium treated group. This is in line with previous studies whereby a significant decrease in spontaneous motor activity and increased anxiety-like behaviours in cadmium-treated rats were reported (Richa *et al.,* 2018; Adaze and Churchill, 2022). Treatment with the extract significantly increased line crossings, rearing frequency, and center square entries as evidenced in rats that received *Launaea taraxacifolia* aqueous extract as a co-treatment with cadmium ($CdCl_2$ + LTAE), implying improved exploratory drive and reduced anxiety. This is in agreement with previous studies whereby a significant increase in line crossings, rearing frequency, and center square entries in animals treated with *Launaea taraxacifolia* were reported (Owoeye and Malomo, 2015; Oyagbemi *et al.,* 2024). These improvements suggest that the extract may exert neuroprotective and anxiolytic effects, possibly through its antioxidant property.

Cresyl fast violet staining is widely used to assess neuronal morphology and the degree of neuronal injury. In this study, the cadmium-exposed rats exhibited significant neuronal degeneration, including shrunken, pyknotic nuclei, cytoplasmic vacuolization and loss of nissl substance. Similar findings have been reported in previous studies, where cadmium exposure led to a breakdown of cellular structures, neuronal dysfunction and loss of neurons in the hippocampus and cortex of animals treated with cadmium (Omotosho *et al.,* 2015; Akpan *et al.,* 2017; Amjad *et al.,* 2019). These histochemical changes are indicative of neurodegeneration and cellular stress resulting from cadmium toxicity. However, in the ameliorative group ($CdCl_2$ + LTAE), a marked preservation of neuronal morphology was observed. The treated rats showed fewer signs of cellular damage, with more well-preserved neurons exhibiting a normal cytoplasmic structure and less nuclear condensation. This supports the study of Olatoye et al. (2024) who reported significant improvement in histological alteration in the brain of rats that received aqueous leaf extracts of *Launaea taraxacifolia* as co-treatment with streptozotocin. According to these findings, *Launaea taraxacifolia* has neuroprotective properties, most likely by reducing oxidative stress and inflammation brought on by cadmium. The notion that the plant extract may aid in maintaining cellular structure and function, shielding neurons from the degenerative effects of cadmium exposure, is supported by the improvement in neuronal integrity seen with cresyl fast violet staining.

Bielschowsky staining, which highlights neurofibrillary tangles and axonal degeneration, was used to evaluate the extent of neurofibrillary changes in the brains of the rats. In the cadmium-exposed group, Bielschowsky staining revealed prominent neurofibrillary degeneration, which is indicative of axonal damage and disrupted neuronal communication, similar to tau-related pathology in AD. The findings in this study is similar with that of Querfurth and Lee (2021) who reported deposition of phospho-tau (p-tau) in the form of neurofibrillary tangles in cadmium-induced cognitive dysfunction in rodents. These changes are consistent with the known effects of cadmium on the central nervous system, where the metal disrupts axonal transport and leads to neuronal disintegration. In contrast, rats treated with *Launaea taraxacifolia* aqueous extract exhibited significantly reduced neurofibrillary degeneration. The neurofibrils in the treated rats appeared more intact, with fewer tangles. This is similar to the study of Olatoye et al. (2024) who reported a reversed plaque and tangles formation in the Bielschowsky sections of brain of animals that received aqueous leaf extracts of *Launaea taraxacifolia* as co-treatment with streptozotocin. This implies that axonal degeneration brought on by cadmium toxicity may be mitigated by *Launaea taraxacifolia*. The antioxidant and anti-inflammatory qualities of the plant extract may contribute to the neuroprotective effects by lowering inflammation and oxidative damage in the central nervous system, thereby preserving axonal integrity.

CONCLUSION

Launaea taraxacifolia aqueous extract demonstrated significant neuroprotective effects against cadmium-induced Alzheimer's disease-like neurodegeneration in the cerebral cortex and hippocampus of Wistar rats. Through behavioural improvement and histological preservation, the extract offers promise as a natural therapeutic agent for neurodegenerative conditions involving heavy metal toxicity or AD-like pathology.

REFERENCES

[1] Adaze, B.E., Churchill, A.I. (2022). Cadmium and Mercury Exposure: Oxidative, Neurobehavioural and Histological Alterations to the Cerebellum of Wistar Rats. *Ibom Medical Journal*, Vol.15, No.2, Pages 141 - 147

[2] Adaze, B.E., Gabriel, O.I. (2022). Attenuation of Oxidative Stress and Cognitive Impairment in Cadmium Chloride-Exposed Wistar Rats Pre-treated with Ethanolic Turmeric Root Extract. *The Journal of Phytopharmacology*, 11(2):118-124

[3] Adinortey, M.B., Justice, K.S., Jeffery, K., Cynthia, A.A., William, E., Lydia, E.K., and Alexander, K.N. (2018). The Ethnopharmacological and Nutraceutical Relevance of *Launaea taraxacifolia* (Willd.) Amin ex C. Jeffrey. Evidence-Based Complementary and Alternative Medicine. Volume 2018, Article ID 7259146, 13 pages https://doi.org/10.1155/2018/7259146

[4] Akingbade, G.T., Ijomone, O.M., Imam, A., Aschner, M., Ajao, M.S. (2022). D-Ribose-L Cysteine attenuates manganese-induced cognitive and motor deficit, oxidative damage, and reactive microglia activation. Environmental Toxicology and Pharmacology, 93:103872 https://doi.org/10.1016/j.etap.2022.103872

[5] Akpan, H.B., Omotoso, O.D., Ogbonna, E., Adelakun, S.A., Oladipupo, F.E., Akande, A.A., Orisadiran, P.K., Olapade, A.R. (2017). Recuperative Action of Aqueous Carica papaya Extract on Cadmium Induced Loss of Nissl Bodies in the Frontal Cortex. *Journal of Applied Life Sciences International*, 13(4): 1-5, 2017; Article no. JALSI.16430

[6] Amjad, K., Muhammad, I., Tahir, M., Junsung, P., Myeong, O.K. (2019). Caffeine Modulates Cadmium-Induced Oxidative Stress, Neuroinflammation, and Cognitive Impairments by Regulating Nrf-2/HO-1 In Vivo and In Vitro, J. Clin. Med., 8, 680; doi:10.3390/jcm8050680

[7] Anyanwu, B.C., Akoh, O.U., and Otuokere, I.E. (2022). Phytochemical Screening and Proximate Analysis of the Leaves of Launaea (Lactuca) Taraxacifolia. J. Chem. Soc. Nigeria, Vol. 47, No. 2, pp 421–432

[8] Babić Leko, M., Langer Horvat, L., Španić Popovački, E., Zubčić, K., Hof, P. R., & Šimić, G. (2023). Metals in Alzheimer's Disease. *Biomedicines*, *11*(4), 1161. https://doi.org/10.3390/biomedicines11041161

[9] Bello, O.M., Abiodun, B.O., Uduma, A.U. (2018). *Launaea taraxacifolia*; a Neglected Vegetable from Nigeria, its Anti-inflammatory and Antioxidant Activities. *ChemSearch Journal* 9(1): 9 – 12,

[10] Koukoui Omédine., et al. (2021). “Combination of the Leaves of Annona muricata, Launaea taraxacifolia and Tridax procumbens: An Herbal Medicine for the Prevention and Treatment of Hypertension, Atherosclerosis and Cardiovascular Diseases". Acta Scientific Pharmaceutical Sciences 5.10: 02-08.

[11] Lazarus, S.S., Adebisi, S.S., Yusuf, T., Abel, N.A., Michael, N.B. (2018). Histological and histochemical assessements on the effect of ethanol fruit extract of Phoenix dactylifera L. (Date Palm) on cerebral cortex of lead acetate

treated wistar rats. Afr. J. Cell. Path. Vol. 10(1), pp. 19

[12] Marreilha Dos Santos, A.P., Lopes Santos, M., Batoreu, M.C., Aschner, M. (2011): Prolactin is a peripheral marker of manganese neurotoxicity. Brain Res. 25, 282–290.

[13] Mertaş, B., Boşgelmez, İ. İ. (2025). The Role of Genetic, Environmental, and Dietary Factors in Alzheimer's Disease: A Narrative Review. *International Journal of Molecular Sciences*, *26*(3), 1222. https://doi.org/10.3390/ijms26031222

[14] Obazelu, P. A., Faluyi, O. (2023). Effect of *Launaea taraxacifolia* Aqueous Leaves Extracts on ICAM 1 and VCAM-1 Gene Expressions in Benzene-Induced Haematotoxicity in Albino Wistar Rats. J. Appl. Sci. Environ. Manage. 27 (12) 2845-2852

[15] Olatoye, A., Olarinde, A., Adesola, O., and Mokolade, I. (2024). "Effects of Aqueous Leave Extracts of *Launaea taraxacifolia* (Willd.) on the Hippocampal Damage in Streptozotocin Induced Diabetic Wistar Rats". International Journal of Tropical Disease & Health 45 (12): 44-59. https://doi.org/10.9734/ijtdh/2024/v45i121611.

[16] Oluwafemi, A.O., Damilare, E.R., Adebola, B.O., Akingbolabo, D, O., Basiru, O.A. (2023). Gallic acid abates cadmium chloride toxicity via alteration of neurotransmitters and modulation of inflammatory markers in Wistar rats. Scientific Reports 13:1577 https://doi.org/10.1038/s41598-023-28893-6

[17] Oluwole, I.A., Oluwadara, B.M., Omotayo, A.E., Esthinsheen, O., Olusanya, A., Ayodeji, A., Ajayi, O. (2023). Neuroprotective Potential of the Methanolic Leaf Extract of *Launaea taraxacifolilia* and Oil of *Dennettia Tripetala* Seed in Sub-chronic Lead Toxicity in Offspring of Rats J Heavy Met Toxicity Dis. 8:006.

[18] Owoeye, O., and Malomo, A.O. (2015). *Launaea taraxacifolia* leaf extract protected against gamma radiation–induced haematological, behavioural and histological alterations in the hippocampus and cerebellum of rats. Arch. Bas. App. Med. 3, 21 – 28

[19] Owoeye, O., Femi-Akinlosotu, O.M., Adejuwon, S.A. (2015). *Launaea taraxacifolia* Aqueous Extract Attenuates Cisplatin Induced Neurotoxicity by Decreasing Oxidative Stress and Neuronal Cell Death in Rats. *Arch. Bas. App. Med*. 3, 71 – 78

[20] Oyagbemi, A.A., Hassan, F.O., Adebiyi, O.E., Adigun, K.O., Folarin, O.R., Ajibade, T.O., et al. (2024). Neuroprotective effect of *Launaea taraxacifolia* against neuroinflammation, memory loss and neurobehavioral deficit in a rat model of hypertension: biochemical and immunohistochemical approaches. J Herbmed Pharmacol. 2024;13(3):390-398. doi: 10.34172/jhp.2024.44768.

[21] Priyanka, S., Sudarshana, M.S., Andrew, A.P., Bindu, D.P., Bobby, T. (2025). Nrf2/Bach1 signaling axis: A promising multifaceted therapeutic strategy for Alzheimer's disease. *Neurotherapeutics* 22 (2025), https://doi.org/10.1016/ j. neurot. 2025.e00586

[22] Qing, Y., Zheng, J., Qin, M. *et al.* (2024). Circulatory trace element variations in Alzheimer's disease: a systematic review and meta-analysis. *Environ Sci Eur* 36, 148. https://doi.org/10.1186/s12302-024-00980-z

[23] Qu, F., Zheng, W. (2024). Cadmium Exposure: Mechanisms and Pathways of Toxicity and Implications for Human Health. *Toxics*, *12*(6), 388. https://doi.org/10.3390/toxics12060388

[24] Querfurth, H., Lee, H.K. (2021). Mammalian/mechanistic target of rapamycin (mTOR) complexes in neurodegeneration. *Mol. Neurodegener*, *16*, 44.

[25] Richa, G., Rajendra, K.S., Ankita, P., Tanuj, S., Yogesh, K.D., Pranay, S., Manjul, P.S., Mohammad, I.S., Aditya, B.P., Vinay, K.K. (2018). Involvement of PKA/DARPP-32/ PP1α and β-arrestin/Akt/GSK-3β Signaling in Cadmium-Induced DA-D2 Receptor Mediated Motor Dysfunctions: Protective Role of Quercetin. Scientific Reports 8:2528, DOI:10.1038/s41598-018-20342-z

[26] Shafri, M.A.M., Abdul, M.M.J., Juliana, M.J., Min, K.K., Hairuszah, I., Farahidah, M. (2012). Cresyl Violet Staining to Assess Neuroprotective and Neuroregenerative Effects of Haruan Traditional Extract Against

Neurodegenerative Damage of Ketamine. *Int J Pharm Pharm Sci, Vol 4, Issue 4, 163-168*

[27] Wen, S., Wang, L., Zou, H., Gu, J., Song, R., Bian, J., Yuan, Y., Liu, Z. (2021). Puerarin Attenuates Cadmium-Induced Neuronal Injury via Stimulating Cadmium Excretion, Inhibiting Oxidative Stress and Apoptosis. *Biomolecules*, *11*(7), 978. https://doi.org/10.3390/biom11070978

[28] Xiqi, H., Ya-nan, M., Jun, P., Zijie, W., Yuchang, L., Ying, X. (2025). Exosomes derived from olfactory mucosa mesenchymal stem cells attenuate cognitive impairment in a mouse model of Alzheimer's disease. BioScience Trends. DOI: 10.5582/bst.2025.01065

[29] Zaman, K., Amina, E., Dilara, A.B., Abdul, R. (2022). Cadmium sources, toxicity, resistance and removal by microorganisms – A potential strategy for cadmium eradication. *Journal of Saudi Chemical Society*, 26, 101569