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Attenuation of Cadmium Chloride-Induced Apoptotic and Structural Alterations in the CA3 Region of the Hippocampus with *Launaea taraxacifolia* Aqueous Extract

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Abstract

Cadmium is a toxic environmental metal known for its damaging effects on brain cells, particularly in the hippocampus, the region responsible for learning and memory. This research investigated the potential neuroprotective effects of *Launaea taraxacifolia* aqueous extract against cadmium chloride ($CdCl_2$)-induced damage in the CA3 area of the hippocampus in male Wistar rats. Thirty-two rats were assigned to four experimental groups: Group A received distilled water, Group B were treated with 5 mg/kg of $CdCl_2$, Group C received 400 mg/kg of *L. taraxacifolia* extract, and Group D were administered 5 mg/kg of $CdCl_2$ followed by 400 mg/kg of the extract. All administrations were given orally for 21 consecutive days. Brain tissues were processed and stained using Hematoxylin and Eosin (H&E) to assess general histology, Cresyl Fast Violet (CFV) to evaluate Nissl substance, Bielschowsky silver stain to examine axonal integrity, and Bax immunostaining to detect apoptotic activity. Rats exposed to $CdCl_2$ showed distorted neuronal architecture, loss of Nissl substance, neuronal degeneration and strong Bax expression, indicating increased cell death. However, animals that received *L. taraxacifolia*, either alone or together with $CdCl_2$ showed preserved neuronal morphology, improved staining intensity, and reduced Bax expression. These findings suggest that *Launaea taraxacifolia* protects hippocampal neurons from cadmium-induced damage, likely by maintaining neuronal structure and regulating apoptosis, as indicated by histological and Bax immunostaining results.

Keywords: *Launaea taraxacifolia*, Cadmium chloride, Hippocampus, Apoptosis, Bax protein.

1.0 Introduction

In recent years, the increasing prevalence of environmental pollutants has raised deep concern about their harmful effects on human health. Among these pollutants, cadmium has drawn particular attention due to its persistence in the environment and its ability to accumulate in body tissues over time [23]. Cadmium chloride, one of the common forms of cadmium exposure, is widely used in industrial and agricultural processes, including battery manufacturing, electroplating, and phosphate fertilizers [7, 8]. Continuous exposure, whether through contaminated food, water, or air, poses serious health risks, even at low concentrations [5].

One of the most sensitive organs affected by cadmium toxicity is the brain, where this heavy metal can disrupt cellular function and trigger oxidative stress, inflammation, and apoptosis [5, 6, 18]. The hippocampus, a region critical for learning and memory, is particularly vulnerable. Within the hippocampus, the CA3 subregion plays a vital role in synaptic transmission and memory processing, making it a key site for studying neuronal injury [17]. Structural damage and apoptotic changes within this area can lead to impaired cognitive functions, emotional imbalance, and neurodegenerative disorders [5].

Given the limitations and side effects of synthetic neuroprotective agents, scientific attention has increasingly shifted toward plant-based alternatives. Many medicinal plants are rich in natural antioxidants and phytochemicals capable of neutralizing free radicals and restoring cellular balance. One such promising plant is *Launaea taraxacifolia* (commonly known as wild lettuce), a leafy vegetable widely consumed in West Africa [4]. Beyond its nutritional value, *Launaea taraxacifolia* has long been recognized in traditional medicine for its antioxidant, anti-inflammatory, hepatoprotective, and detoxifying properties [1, 13]. While *Launaea taraxacifolia* has shown promising neuroprotective effects in other forms of brain damage, its protective effects against cadmium-induced hippocampal damage remain uninvestigated. This study, therefore, seeks to evaluate the protective role of *Launaea taraxacifolia* aqueous extract against cadmium chloride–induced apoptotic and structural alterations in the CA3 region of the hippocampus. By investigating the histochemical changes associated with cadmium toxicity and the possible ameliorative effects of the extract, this research aims to bridge the gap between traditional knowledge and modern neurotoxicology.

Ultimately, the findings from this study could provide valuable insights into the use of natural plant extracts as cost-effective, accessible, and sustainable alternatives for preventing or mitigating heavy-metal-induced neurodegeneration. Understanding such mechanisms not only contributes to the growing field of neuroprotection but also supports the development of safer therapeutic strategies for preserving brain health in an increasingly polluted world.

2.0 Materials and Methods

2.1 Preparation and Concentration 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 [15]. After soaking 300g of the powdered leaves in 4 liters of distilled water that had been continuously heated to 60ºC for 24 hours, the leaves were filtered through filter paper. A rotary evaporator was used to concentrate the filtrate, and the yield (Y) was computed using the following formula:

$$Y\ (\%) = (\text{Mass of extract}) / (\text{Mass of plant material used}) \times 100$$

The stock solution, which was made by diluting 6 g of extract with 48 ml of distilled water at 3-day intervals, was used to determine the dosage of the dried extract that was given.

2.2 Experimental Animals

Thirty-two (32) adult male Wistar rats, weighing between 200 and 250 ± 15 g were used for this study. The animals were maintained under standard laboratory conditions with unrestricted access to food and water. All experimental procedures adhered to established ethical standards and received approval from the Institutional Animal Ethics Committee.

2.3 Experimental Design

The thirty-two (32) Wistar rats were randomly divided into four groups;

Table 1: Animal Grouping and Drug Administration

GROUPS	TREATMENT	ROUTE OF ADMINISTRATION
Group A (Control)	Distilled water	Oral gavage
Group B	5 mg/kg $CdCl_2$ only	Oral gavage
Group C	400 mg/kg LTAE only	Oral gavage
Group D	5 mg/kg $CdCl_2$, followed immediately by 400 mg/kg LTAE	Oral gavage

2.4 Histological Analysis

Brain tissues were preserved in 10% neutral buffered formalin and processed using standard histological procedures. Sections were stained with hematoxylin and eosin to examine the general neuronal architecture [12]. Cresyl fast violet staining was done by the method of [19] for demonstration of neurons and Nissl bodies. Bielschowsky staining was done by the method of [10] for the visualization of nerve fibres, axons, neurofibrils and senile plaque. Stained sections were observed under a light microscope.

2.5 Bax Immunohistochemistry

Immunohistochemical analysis was conducted following the procedure outlined by [12].

3.0 RESULTS

3.1 Effects of LTAE on the Histology of the Brains of Wistar Rats

Plate 1 represent the photomicrographs of the Haematoxylin and Eosin (H&E) staining of the CA3 region of the hippocampus of Wistar rats across groups. In the control group, the CA3 region showed normal pyramidal neurons with clear nuclei and well-organized layers. $CdCl_2$ exposure caused marked neuronal shrinkage, and disorganization of the pyramidal layer. Rats co-treated

with *L. taraxacifolia* ($CdCl_2$+LTAE) showed a notable reduction in these alterations, with hippocampal neurons retaining near-normal morphology.

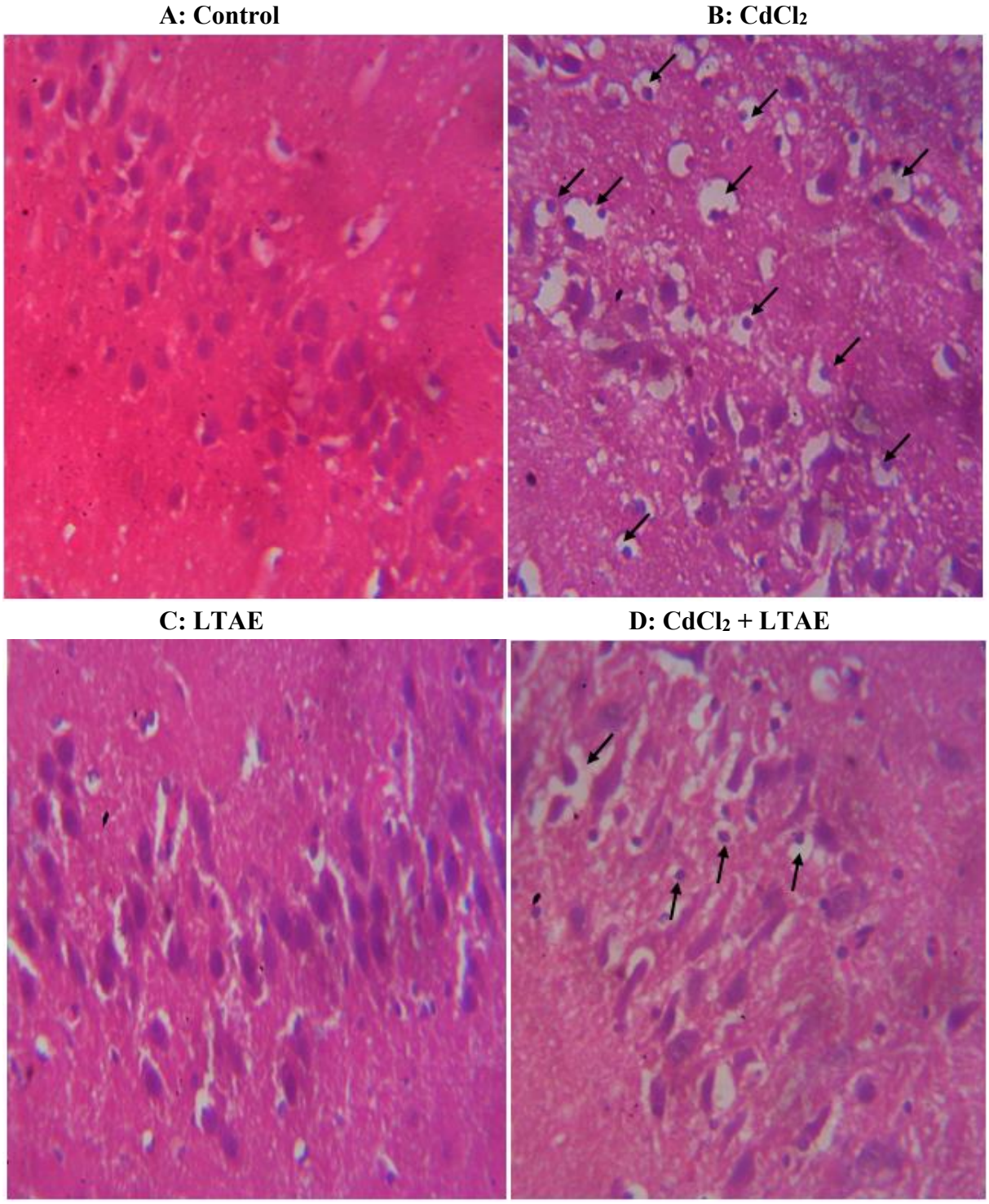


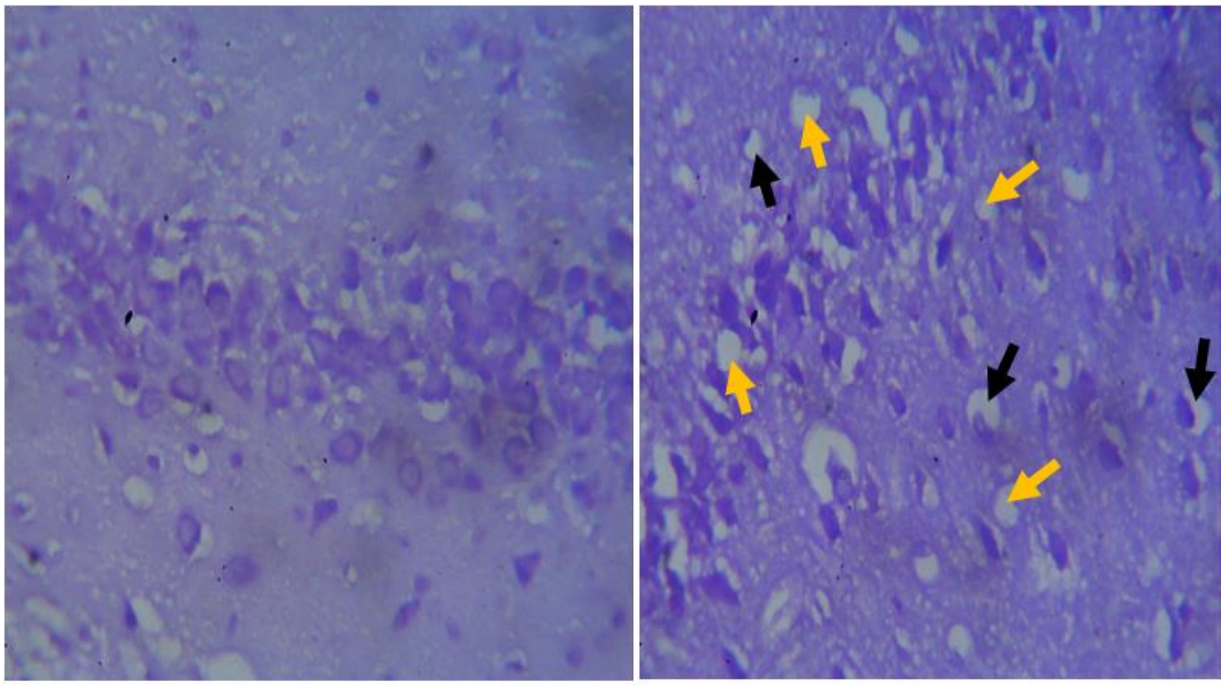
Plate 1: Effects of LTAE on $CdCl_2$-induced histological changes in the CA3 region of the hippocampus of Wistar rats (H&E, 400X). The pyramidal neurons in the group A displayed normal

morphological features. In contrast, group B showed marked degenerative changes, including pyknotic nuclei (black arrows) and a reduced neuronal layer. The group treated with *Launaea taraxacifolia* extract (group C) alone exhibited well-organized neuronal structures, while group D showed a noticeable reduction in pyknotic cells (black arrows) compared to group A. ($CdCl_2$ = Cadmium chloride; LTAE = *Launaea taraxacifolia* aqueous extract)

3.2 Effects of LTAE on Cresyl Fast Violet Staining of the Brains of Wistar Rats

Plate 2 represent the photomicrographs of the Cresyl fast violet staining of the CA3 region of the hippocampus of Wistar rats across groups. CFV staining showed abundant Nissl granules in control neurons. In $CdCl_2$-treated animals, there was a marked loss of Nissl substance (chromatolysis) and karyolysis, indicating neuronal injury. Co-treatment with *L. taraxacifolia* preserved Nissl bodies and maintained normal staining intensity ($CdCl_2$+LTAE).

A: Control **B: $CdCl_2$**



C: LTAE **D: $CdCl_2$ + LTAE**

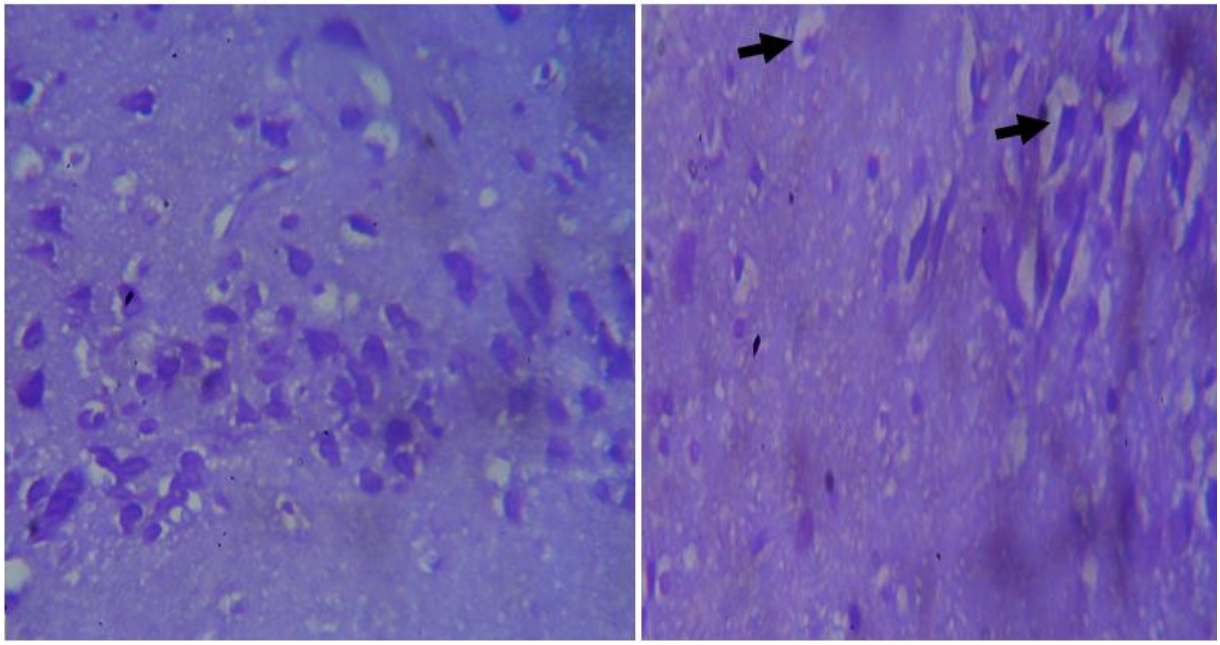


Plate 2: Effects of LTAE on $CdCl_2$-induced histochemical changes in the pyramidal layer of the CA3 region of the hippocampus of Wistar rats (CFV, 400X). The CA3 region of the control group (group A) exhibited intensely chromatophilic pyramidal neurons with normal morphology. In the $CdCl_2$ treated group (group B), neuronal degeneration was evident, characterized by chromatolysis (yellow arrows) and karyolysis (black arrows). The group treated with *Launaea taraxacifolia* extract (group C) showed well-preserved, highly chromatophilic pyramidal cells, while $CdCl_2$ exposed rats treated with LTAE (group D) demonstrated improved neuronal staining properties with a marked reduction in karyolysis and chromatolysis. ($CdCl_2$ = Cadmium chloride; LTAE = *Launaea taraxacifolia* aqueous extract)

3.3 Effects of LTAE on Bielschowsky Staining of the Brain of Wistar Rats

Plate 3 is the photomicrograph of the Bielschowsky staining of the CA3 region of the hippocampus of Wistar rats across groups. Microscopic evaluation revealed that both the control and LTAE-only treated groups displayed normal dark yellow to brown-stained neurons against a yellow background across all brain regions. In contrast, the $CdCl_2$-treated group exhibited marked degenerative changes, including the presence of neurofibrillary tangles and neuronal shrinkage when compared to the control. The $CdCl_2$ + LTAE co-treated group showed better-preserved neuronal structures with fewer neurofibrillary tangles than the $CdCl_2$ group.

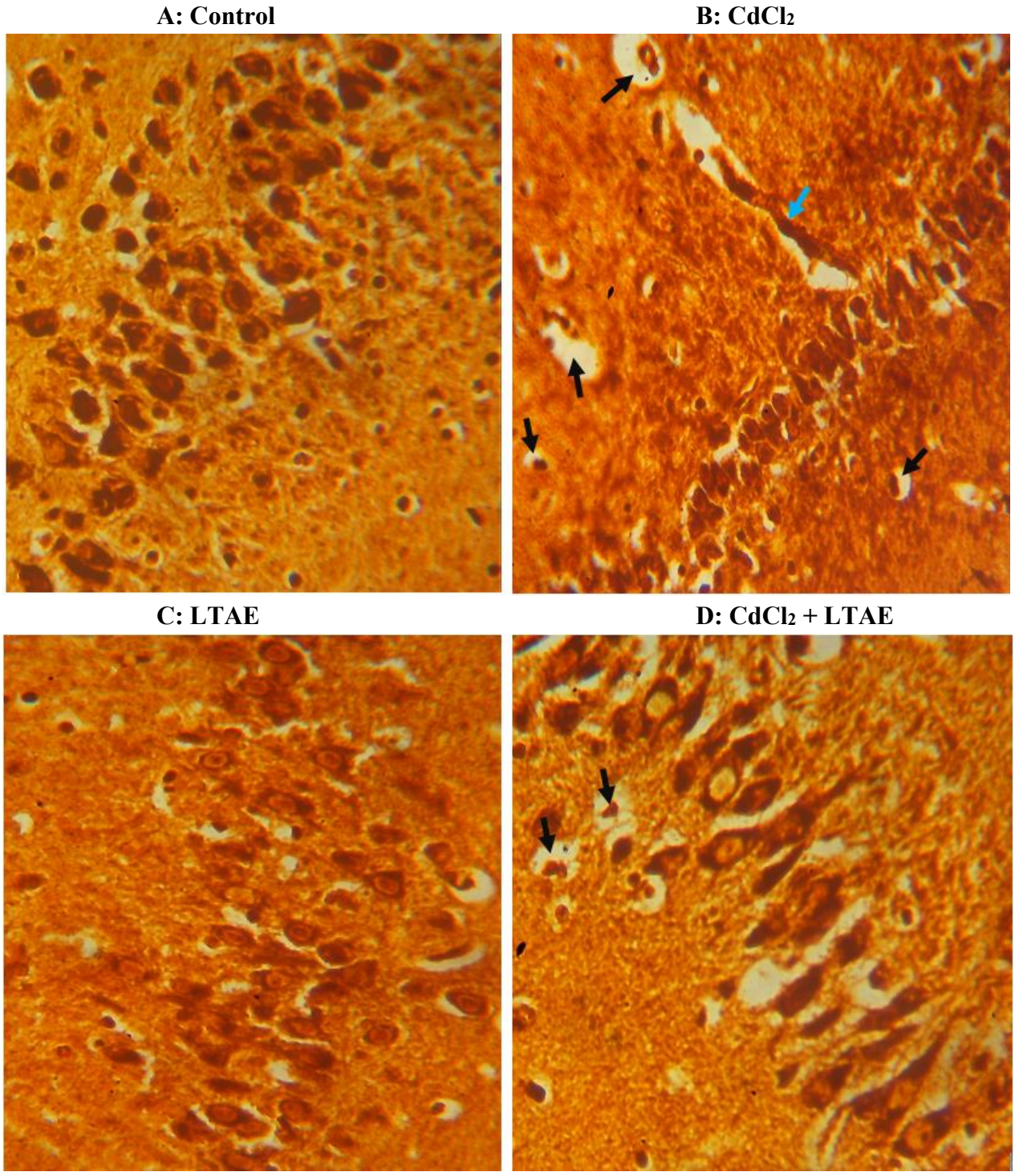


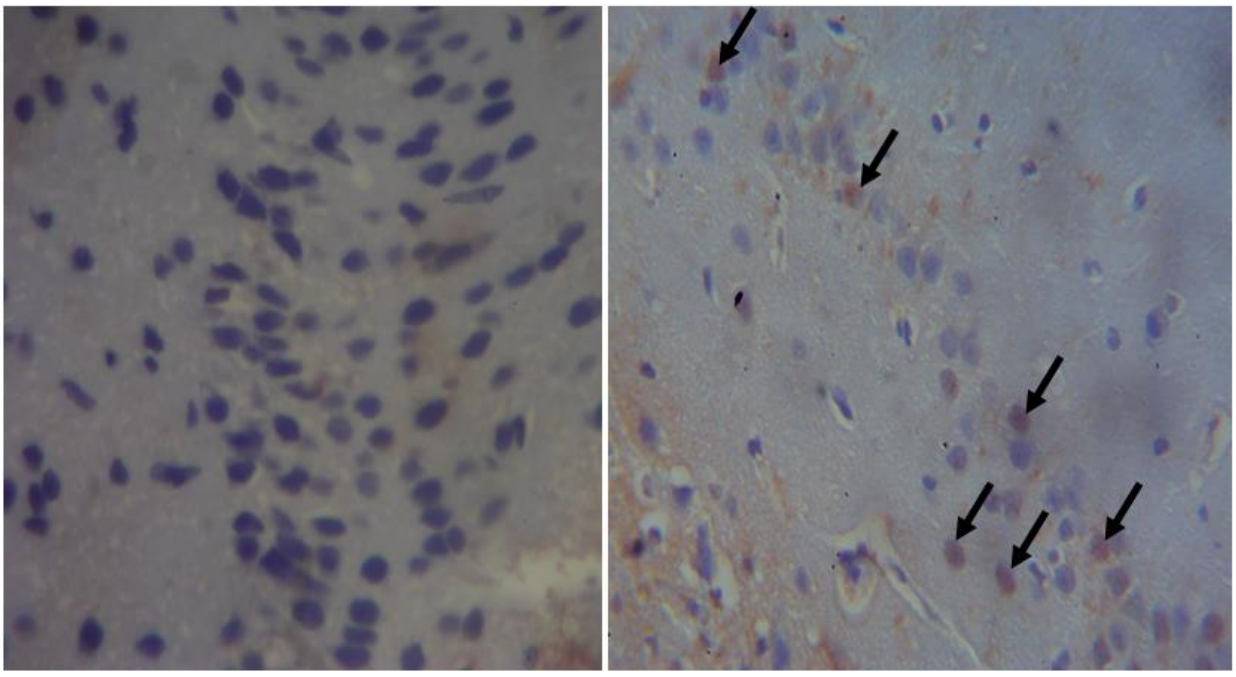
Plate 3: Effects of LTAE on $CdCl_2$-induced histochemical changes in the CA3 region of the hippocampus of Wistar rats (Bielschowsky, 400X). The CA3 region of the control group (group A) showed normally stained brown neurons against a yellow background. In the $CdCl_2$-treated group (group B), neurofibrillary tangles (blue arrow) and neuronal shrinkage (black arrows) were prominently observed. The group treated with LTAE alone (group C) displayed normal neuronal

staining similar to the control, while the $CdCl_2$ + LTAE co-treated group (group D) exhibited a noticeable reduction or absence of neurofibrillary tangles. ($CdCl_2$ = Cadmium chloride; LTAE = *Launaea taraxacifolia* aqueous extract).

3.4 Effects of LTAE on the Expression of Bax in the Brains of Wistar Rats

Plate 4 represent the photomicrograph of Bax immunostaining of the CA3 region of the hippocampus of Wistar rats across groups. Microscopic examination of the control and the LTAE-alone treated group shows normal bax immunoactivity in the hippocampus. Strong Bax immunoreactivity was observed in $CdCl_2$-treated neurons. In contrast, *L. taraxacifolia*-treated (LTAE) and co-treated rats ($CdCl_2$ + LTAE) showed weak Bax expression.

A: Control **B: $CdCl_2$**



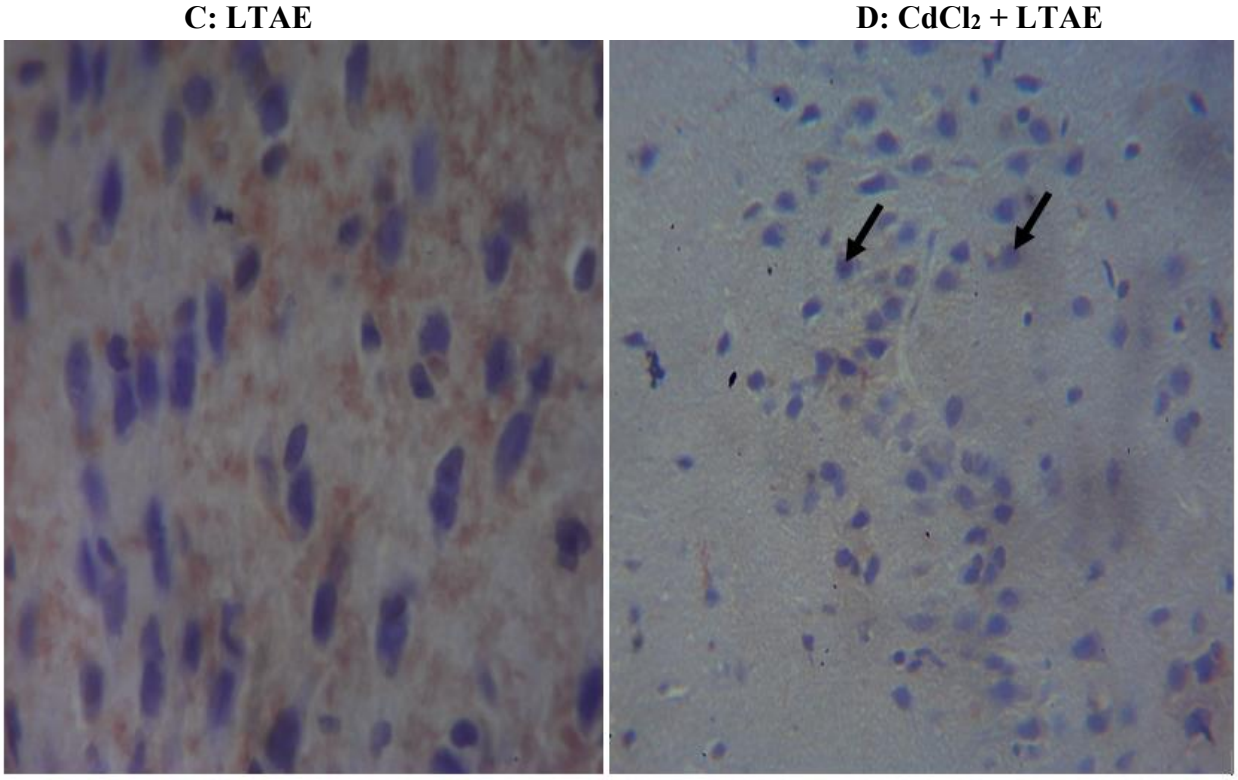


Plate 4: Effects of LTAE on $CdCl_2$-induced immunohistochemical changes in the CA3 region of the hippocampus of Wistar rats (Bax, 400X). The CA3 region of the control group (group A) presents minimal Bax expression. The $CdCl_2$ group (group B) was characterized by strong Bax antibody immunostaining (black arrows). Also, LTAE treated group (group C) was characterized by a weak Bax antibody expression. Treatment of $CdCl_2$ rats with LTAE (group D) shows a decrease in Bax expression (black arrows). ($CdCl_2$=Cadmium chloride; LTAE= *Launaea taraxacifolia* aqueous extract).

4.0 Discussion

The present study examined the protective effect of *Launaea taraxacifolia* aqueous extract on cadmium chloride–induced neuronal and structural alterations in the hippocampal CA3 region. The results clearly show that exposure to cadmium chloride produced histopathological changes consistent with neuronal injury, while co-treatment with *L. taraxacifolia* effectively preserved the structural integrity of the hippocampal neurons.

Cadmium is a well-recognized neurotoxicant capable of crossing the blood-brain barrier and accumulating within brain tissues [3]. Once deposited, it disrupts cellular homeostasis, interferes with neuronal communication, and leads to progressive cell degeneration [5, 22]. The hippocampus, particularly the CA3 region, is known to be highly susceptible to toxic insults because of its dense network of excitatory neurons and its central role in learning and memory [2].

In the current study, H&E-stained sections from cadmium-treated animals revealed characteristic features of neurodegeneration, including distorted pyramidal layers, neuronal shrinkage, and pyknotic nuclei. The pathological changes observed in the $CdCl_2$-treated group are consistent with previous studies whereby distorted tissue cytoarchitecture and damaged nuclei of cells in the brain of cadmium treated animals were reported [17, 21]. These alterations are typical of cellular damage caused by heavy metal exposure and suggest that cadmium severely impairs hippocampal cytoarchitecture. However, sections from animals co-treated with *Launaea taraxacifolia* extract displayed well-preserved cellular organization, with most pyramidal neurons appearing structurally normal and clearly defined as seen in the ameliorative group ($CdCl_2$ + LTAE). This supports the study of [16] who reported significant improvement in histological alteration in the brain of rats that received *Launaea taraxacifolia* aqueous extract as co-treatment with lead. [11] also reported that alterations in the brain of streptozotocin-induced diabetic Wistar rats were normalized upon *Launaea taraxacifolia* ethanolic extract supplementation. This observation indicates that the extract provided substantial protection against cadmium-induced neuronal distortion.

Cresyl Fast Violet staining, which targets Nissl substances, further highlighted the neuroprotective potential of the extract. In the cadmium-treated group, there was marked chromatolysis, loss of Nissl granules, and cytoplasmic dissolution, evidence of disrupted protein synthesis and neuronal distress. 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 of animals treated with cadmium [9, 14]. In contrast, the extract-treated sections showed a near-normal pattern of Nissl substance distribution. The reappearance of well-stained granules implies improved neuronal integrity and restored synthetic activity. This supports the study of [11] 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. This observation supports the idea that *L. taraxacifolia* enhances the maintenance of neuronal metabolic function and promotes recovery of affected cells.

The Bielschowsky staining provided complementary evidence on axonal integrity. Cadmium exposure resulted in axonal fragmentation, neurofibrillary tangles and neuronal shrinkage, suggesting deterioration of neuronal connectivity. Such structural breakdown could contribute to impaired synaptic transmission and memory dysfunction often associated with hippocampal injury. Remarkably, animals treated with *L. taraxacifolia* aqueous extract showed continuous, well-defined axonal fibers with minimal signs of degeneration. This is consistent with the findings 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 preservation of neuronal processes implies that the extract helps to maintain cytoskeletal stability and prevents excessive axonal damage, which is essential for normal hippocampal function.

The immunohistochemical analysis of Bax expression offered further insight into the mechanism of neuronal protection. Bax is a pro-apoptotic protein that facilitates programmed cell death by enhancing the permeability of the mitochondrial membrane. The intense Bax immunoreactivity observed in the cadmium-treated group confirms the activation of apoptotic pathways in response to toxic stress. This is similar to the study of [20] whereby up-regulation of Bax expression in cadmium-treated rats was reported. However, sections from animals treated with *L. taraxacifolia* extract exhibited markedly reduced Bax expression, suggesting suppression of apoptosis and improved neuronal survival. This downregulation of Bax is consistent with the histological evidence of reduced degeneration, indicating that the extract possibly interferes with apoptosis initiation or progression at the cellular level.

Altogether, the results from all staining techniques strongly suggest that *Launaea taraxacifolia* aqueous extract provided structural protection against cadmium chloride–induced hippocampal injury. The extract appeared to preserve neuronal structure, sustain Nissl substance integrity, maintain axonal continuity, and reduce apoptotic activity in the CA3 region. These findings lend scientific support to the traditional use of *L. taraxacifolia* as a natural remedy for detoxification and tissue protection. More importantly, they highlight the potential of this indigenous plant as a cost-effective neuroprotective agent against heavy-metal-induced neuronal damage.

5.0 Conclusion

This study revealed that *Launaea taraxacifolia* aqueous extract effectively protected the hippocampal CA3 region from cadmium chloride–induced structural and apoptotic damage. Cadmium exposure caused marked neuronal degeneration, loss of Nissl substance, axonal disruption, and elevated Bax expression, while treatment with *L. taraxacifolia* preserved neuronal architecture and reduced apoptotic activity. These findings suggest that the extract possesses neuroprotective potential, likely due to its reported bioactive constituents that support neuronal stability and survival. Although further studies are needed to clarify its exact mechanisms and strengthen the reliability of the findings, particularly through the inclusion of appropriate positive controls, *Launaea taraxacifolia* still shows promising potential as a natural agent for mitigating heavy-metal-induced neurotoxicity.

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Conflict of Interest

The authors declare no conflict of interest.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, EOA.

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Authors' Contribution

TSO: Conceptualization, supervision, project administration, proofreading and final manuscript editing. **GTA**: Conceptualization, supervision, methodology, project administration. **EOA**: Conducted experiments, data collection, data analysis, and writing-original draft.

Ethical Approval

All procedures were in accordance with the National Institute of Health Guidelines for the Care and Use of Laboratory Animals and approved by the ethical standards of the institution (FUTA/ETH/25/235).

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