Ethanolic Leaf Extract of Aloe Barbadensis (Aloe Vera) Mitigates Mercury Induced Alzheimer –Like Symptoms on Basal Ganglia of Albino Wistar Rats

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ABSTRACT

Mercury exposure has been linked with numerous neurological disorders that frequently trigger Alzheimer's disease through oxidative stress processes. This study aims to determine the ameliorative potential of Aloe barbadensis on mercury induced Alzheimer- like symptoms on basal ganglia of wistar rats. Thirty-five wistar rats with average weight 150g were randomly divided into five groups designated A-E with seven rats per group. Group A served as the control and did not receive any treatment, group B received 5mg/kg mercury chloride only for three weeks, group C received 500mg/kg of ethanolic extract of Aloe barbadensis for 3 weeks, groups D and E received 5mg/kg of mercury chloride for 3 weeks followed by 250mg/kg and 500mg/kg of ethanolic extract of Aloe barbadensis for 3 weeks respectively. All administrations were via oral gavage. Anxiety index and recognition memory were evaluated using open field and novel object recognition tests. Blood was obtained via ocular puncture for serum estimation of superoxide dismutase (SOD), malondialdehyde (MDA) levels. Brain tissue obtained were homogenized for estimation of Acetylcholinesterase (AChE) and glutamate levels and also processed for routine Hematoxylin and eosin and silver Beilschowsky staining. Results of the neurobehavioural tests showed significant ($P<0.05$) increase in anxiety indexwhen comparand significant decrease ($P<0.05$) in recognition index in group B. There was significant ($P<0.05$) decrease in SOD, AChE, glutamatelevels in group B compared with groups A, C, D and E while there was a significant increase ($P<0.05$) in MDA levels in group B. Histological study of the basal ganglia showed pyknotic nuclei in group B while silver beilschowsky stain revealed amyloid plaques deposition in group B. These results revealed that mercury chloride caused oxidative stress, anxiety, reduced AChE and glutamate levels, pyknosis and deposition of amyloid plaques on the basal ganglia and Aloe Barbadensis ethanolic extract mitigated these effects and may be useful in the management of Alzheimer –like symptoms.

Keywords— Mercury chloride, oxidative stress, amyloid plaques, Alzheimer's disease, Aloe barbadensis

INTRODUCTION

Environmental exposure to toxic chemicals has been strongly associated with neurotoxicity, particularly through mechanisms involving oxidative stress and lipid peroxidation in brain tissues. Among these environmental pollutants, mercury chloride ($HgCl_2$) is a well-known neurotoxicant that affects the central nervous system and has been implicated in the development of several neurological disorders [7], including Parkinson's disease, Alzheimer's disease and Huntington's disease. Mercury, a heavy metal of global concern is introduced into the ecosystem through both natural and anthropogenic activities, leading to its persistence and bioaccumulation in humans and animals. Due to its unique physicochemical properties, mercury deeply affects human health and has been linked to cognitive dysfunction and other neurological disorders related to neuroinflammation and oxidative stress processes [5], resulting in neuropathological diseases such as Alzheimer's disease and other neurodegenerative diseases.

Alzheimer's disease is a multifactorial neurological condition associated with neuropathological and neurobehavioral changes, including cognition and memory loss [12]. The basal ganglia an essential brain region is associated with reward, cognition and motor control. It acts as the gate-keeping mechanism for motor

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movement initiation [15], deciding which actions to execute or inhibit. It is a primary site of dysfunction in both Parkinson's disease and Huntington's disease.

Increasing research indicates that mercury-related neurotoxicity may compromise the functional integrity of the basal ganglia. Given this region's critical involvement in both motor and cognitive functions, it is vital to explore how mercury exposure affects its neuronal health, particularly in relation to Alzheimer's disease-like symptoms. The pathogenesis of mercury-induced neurotoxicity is primarily associated with oxidative stress, leading to neuronal damage, neurotransmitter imbalances and cognitive deficits characteristic of Alzheimer's disease. Oxidative stress disrupts the delicate balance of antioxidants, such as superoxide dismutase (SOD) and elevates lipid peroxidation markers, including malondialdehyde (MDA). It also impairs enzymes critical for neural function, including acetylcholinesterase (AChE). Additionally, mercury accumulation contributes to pathological changes such as neuronal pyknosis and amyloid plaque deposition, which are hallmarks of Alzheimer's pathology. Thus, Alzheimer's disease is linked to dementia, characterized by chronic behavioral changes such as apathy, aggressiveness, depression, and lack of social activities [23].

Antioxidants play a vital role in reducing oxidative stress markers linked to reactive oxygen species formation. In recent years, natural antioxidants have attracted attention for their neuroprotective properties against heavy metal-induced neurotoxicity. Medicinal plants are increasingly recognized for their potent antioxidant properties, which contribute significantly to their therapeutic value in addressing a diverse array of health conditions, including neurodegenerative disorders like Alzheimer's disease and other neurological impairments ([20],[27]). These plants are rich in bioactive phytochemicals—such as flavonoids, alkaloids, terpenoids and polyphenols—that not only neutralize harmful free radicals but also modulate key biological pathways involved in inflammation, immune response, and cellular repair.

Their multifaceted healing potential stems from a synergistic blend of pharmacological actions. Anti-inflammatory compounds help reduce neuroinflammation, a hallmark of many brain disorders. Antioxidants protect neurons from oxidative stress, which is implicated in the progression of Alzheimer's and Parkinson's diseases. Immunomodulatory agents enhance the body's defense mechanisms, while anticancer and antimicrobial constituents broaden their application to oncology and infectious disease management [19].Beyond their biochemical effects, medicinal plants offer a holistic approach to healing, often aligning with traditional medicine systems that emphasize balance and restoration. As interest grows in natural and integrative therapies, these plants continue to be explored not only for symptom relief but also for their potential to slow disease progression and improve quality of life in chronic neurological conditions.

Aloe barbadensis miller (Aloe vera) has demonstrated potential in mitigating oxidative damage and improving neurological outcomes in various experimental models. It is a perennial green herb native to North Africa, the Middle East, Southern Mediterranean, and Canary Islands [22]. Aloe barbadensis contains active compounds such as aloe-emodin, aloin, aloesin, emodin, and acemannan, linked to pharmacological effects like anticancer, antioxidant, antidiabetic and antihyperlipidemic actions ([8],[14]).

This study investigates whether the ethanolic leaf extract of Aloe barbadensis (Aloe vera) can counteract the neurodegenerative effects of mercury chloride exposure, which is known to induce Alzheimer-like symptoms in the basal ganglia of albino Wistar rats. Mercury chloride is a potent neurotoxin that disrupts neuronal function primarily through oxidative stress, leading to behavioral impairments, biochemical imbalances, and structural brain damage that resemble the pathology of Alzheimer's disease.

To address this, the study evaluates the extent to which Aloe barbadensis extract can restore normal brain function by targeting key markers of neurotoxicity. These include behavioral parameters such as anxiety and memory performance, assessed through open field and novel object recognition tests. On a biochemical level, the research measures antioxidant enzyme activity (superoxide dismutase), lipid peroxidation (malondialdehyde) and neurotransmitter-related enzymes (acetylcholinesterase and glutamate), which are critical indicators of oxidative stress and synaptic integrity.

Additionally, the study examines histopathological changes in the basal ganglia, focusing on neuronal degeneration (evidenced by pyknotic nuclei) and the presence of amyloid plaques, which are hallmark features of Alzheimer's disease. By comparing treated and untreated groups, the research aims to determine whether Aloe

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barbadensis can mitigate these effects, thereby offering a potential natural therapeutic strategy for managing mercury-induced neurodegeneration and Alzheimer-like conditions.

MATERIALS AND METHODS

Experimental animals

The study was conducted in the animal house unit, Department of Human Anatomy, Faculty of Basic medical Sciences, Chukwuemeka Odumegwu University, Uli campus. With 35 adult male wistar rats weighing 130 – 150g.The rats were kept in standard cages at room temperature of 27±2°C and was maintained on 12-hours light and dark cycles to maintain the normal circadian rhythm fed with standardized pellet grower's feed and distilled water ad libitum. The rats were acclimatized for two weeks for physiological adaptation to the animal house before administering mercury chloride and ethanol extracts of Aloe barbadensis miller.

Plant extract preparation

Aloe barbadensis miller (Aloe-vera) was obtained from a local farm in Nnewi North and was washed to remove dirt. The dried aloe-vera was milled into a coarse powdered form using a local grinder. About 250 g each of the dried forms of the aloe-vera was macerated in 1000 ml of 95% absolute ethanol for 48 hours. It was filtered using a clean white cloth and further filtration using Whatman No 1 filter paper. The filtrate was concentrated using a rotatory evaporator and dried further using a laboratory oven at 45ºC into a gel-like form. The extract was preserved in airtight container and kept in a refrigerator for further usage.The extraction method was done with modifications as described according to the method employed by [1].

Ethical Approval

This was obtained from the ethical committee, faculty of basic medical sciences Chukwuemeka Odumegwu Ojukwu University, Uli campus in compliance with the relevant laws and institution's guidelines.

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee**.**

Subacute Toxicity Study

All animals were housed under same environmental conditions throughout the study. Thirty-five rats were randomly assigned into five groups (n = 7). Group A served as the negative control and received feed and water only. Group B, received 5 mg/kg of mercury chloride for 3 weeks. Group C was administered 500 mg/kg of Aloe barbadensis extract for 3 weeks. Group D and E received 5 mg/kg of mercury chloride for 3 weeks, followed by 250 mg/kg and 500mg/kg of Aloe barbadensis extract for another 3 weeks respectively. All administrations were done daily via oral gavage.

Twenty-four hours after the final treatment, animals were subjected to open field test followed by object recognition test. Blood was collected via ocular puncture. Serum was separated and used for superoxide dismutase and malondialdehyde assays. The animals were anesthetized using 50mg/kg ketamine.Brain tissue obtained were homogenized for estimation of Acetylcholinesterase (AChE) and glutamate levels and also processed for routine Hematoxylin and eosin and silver Beilschowsky staining.

Statistical Analysis

Data were analyzed using GraphPad Prism version 9.5.1. One-way ANOVA followed by Fisher's Least Significant Difference (LSD) post hoc test was used to analyze brain levels of MDA, SOD, glutamate, acetylcholinesterase activity, anxiety index, and recognition memory. Histological findings, including amyloid plaque deposition, were also evaluated descriptively. Results were expressed as mean ± standard error of the mean (SEM), and differences were considered statistically significant at $p \leq 0.05$.

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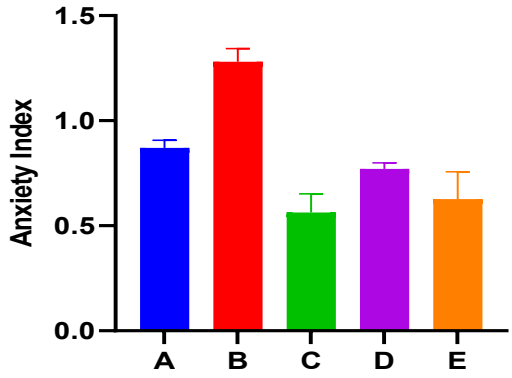
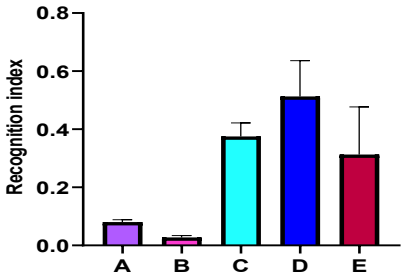
RESULTS

Figure 1: Effect of ethanolic extract of Aloe barbadensis Miller on anxiety index following mercury chloride exposed rats.



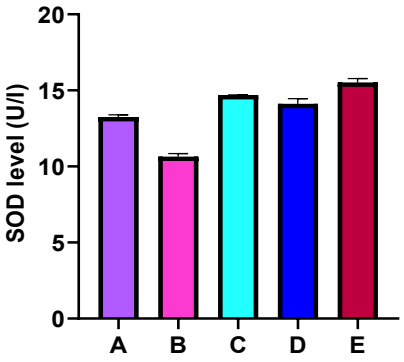
Anxiety index results showed that there was a significant increase ($P<0.05$) in anxiety index in group B compared to group A and the aloe barbadensis treated groups while there was a decrease in anxiety index in group C compared with group A. Figure 1

Figure 2: Effect of ethanolic extract of Aloe barbadensis Miller on recognition index following mercury chloride exposed rats.



Results of the recognition index showed that there was a significant increase($P<0.05$) in recognition index in groups C, D and E compared with groups A and B while there was no significant difference between the recognition index of group B compared with group A. Figure 2

Figure 3: Effect of ethanolic extract of Aloe barbadensis Miller on SOD level following mercury chloride exposed rats.



SOD levels in group B had a significant decrease($P<0.05$). Groups C, D, and E had a significant increase compared to group A. However, the serum SOD activities in groups C, D, and E had a significant increase compared to group B. Figure 3

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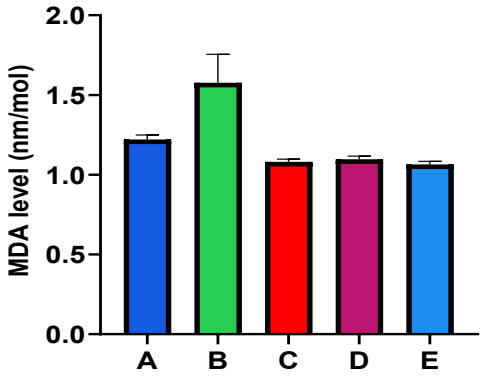
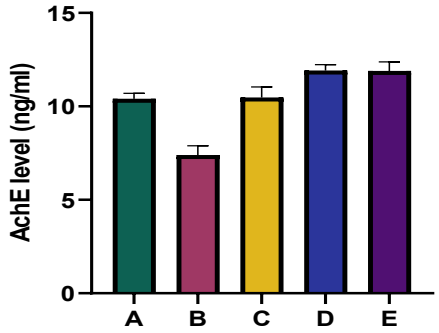
Figure 4: Effect of ethanolic extract of Aloe barbadensis Miller on MDA level following mercury chloride exposed rats.



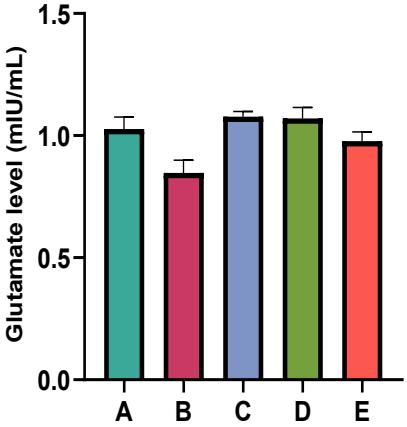
Result shows a significant increase ($p<0.05$) in the MDA level in group B while groups C,D,E showed a decrease when compared to group A. Figure 4

Figure 5: Effect of ethanolic extract of Aloe barbadensis Miller on AchE level following mercury chloride exposed rats.



The acetylcholine esterase activity reveals significant increase ($p<0.05$) in the AChE activity in groups C, D, and E compared to group B. While group C had no significant difference compared to group A. Figure. 5

Figure 6: Effect of ethanolic extract of Aloe barbadensis Miller on glutamate level following mercury chloride exposed rats.



Result reveals a decrease in the glutamate level in group B and E, groups C and D had an increase when compared to group A, which had significant difference in group B($P<0.05$). However, the glutamate level shows a significant increase in groups C and D($P<0.05$). Group E had no significant difference compared to group B. Figure 6

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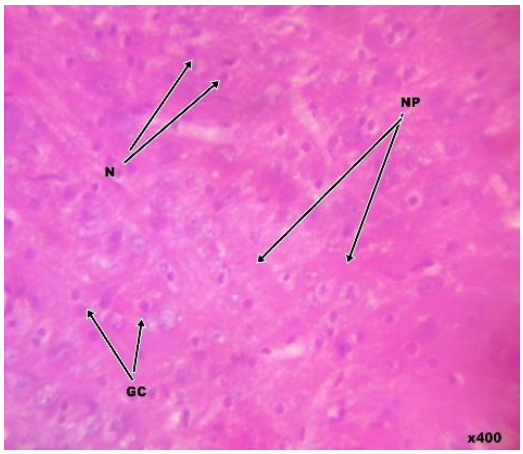
Histological Studies Results

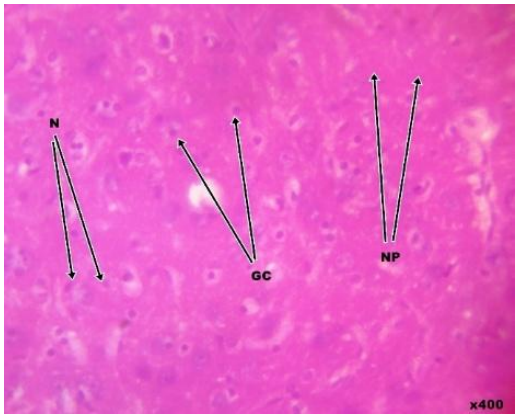
Hematoxylin and Eosin (H &E) staining

Figure 7: Group A (H&E staining)



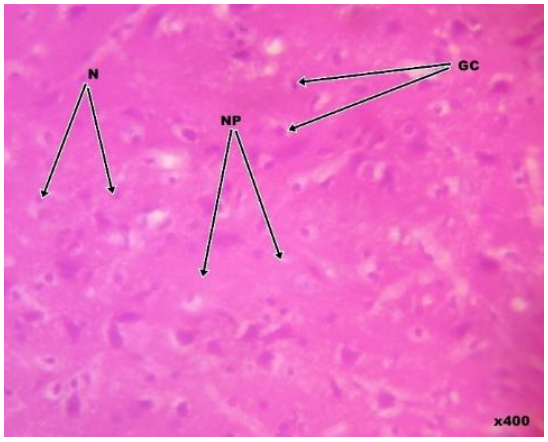
Group A received feed and water ad libitum: Photomicrograph of basal ganglia show some densely packed medium neurons (N), mainly caudate and putamen (collectively known as the striatum). Elsewhere, there are numerous glial cells (GC). The background matrix shows a dense neuropil (NP). H & E (x400). Figure 7

Figure 8: Group B (H&E staining)



Group B received 5mg/kg of mercury chloride. A photomicrograph section of the basal ganglia shows pyknotic nuclei with moderate reduction of neurons (N) and the glial cells. H & E (x400). Figure 8

Figure 9: Group C (H&E staining)



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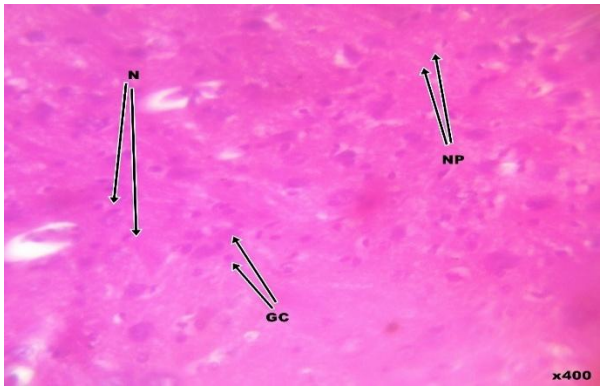
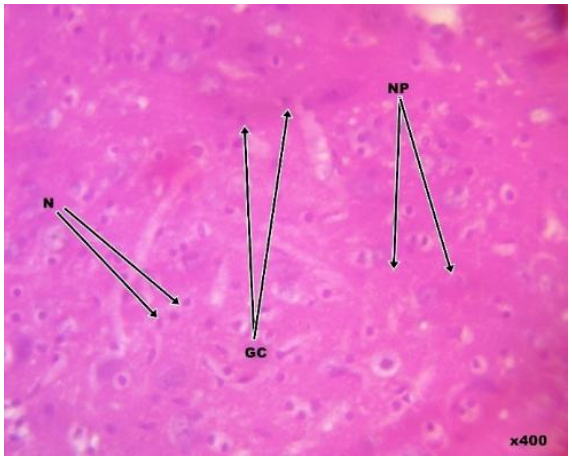
Group C (500 mg/kg of Ethanolic extract ofaloe barbadensis): A photomicrograph section of the basal ganglia showing numerous large neurons (N) and the glial cells. Stained with H & E (x400). Figure 9

Figure 10: Group D (H&E staining)



Group D (5mg/kg of HgCl2 for 3-weeks + 250 mg/kg of Ethanolic extract of aloe barbadensis): A photomicrograph section of the Basal ganglia shows moderate reduction of neurons (N) and the glial cells. Stained with H & E (x400). Figure 10

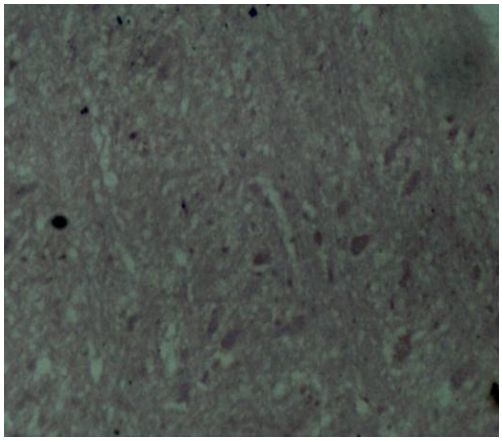
Figure 11: Group E (H&E staining)



Group E (5mg/kg of HgCl2 for 3-weeks + 500 mg/kg of Ethanolic extract ofaloe barbadensis): Photomicrograph section of the Basal ganglia showing normal neurons (N) and glial cells. Stained with H & E (x400). Figure 11

Silver Beilschowsky Stain

Figure 12: Group A (Silver Beilschowsky Stain).



Group A received feed and water ad libitum: A section of brain (Basal ganglion) section of albino rat showing

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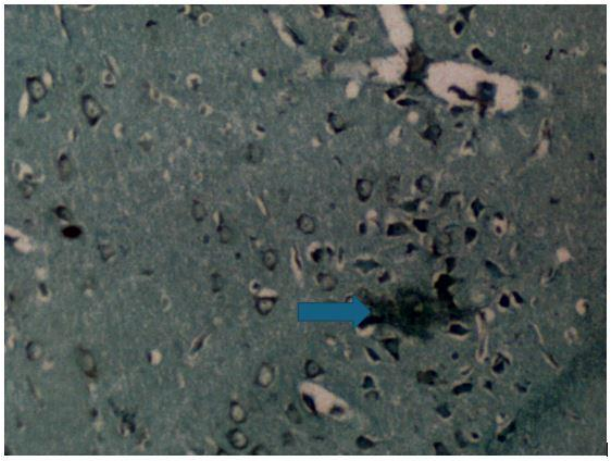
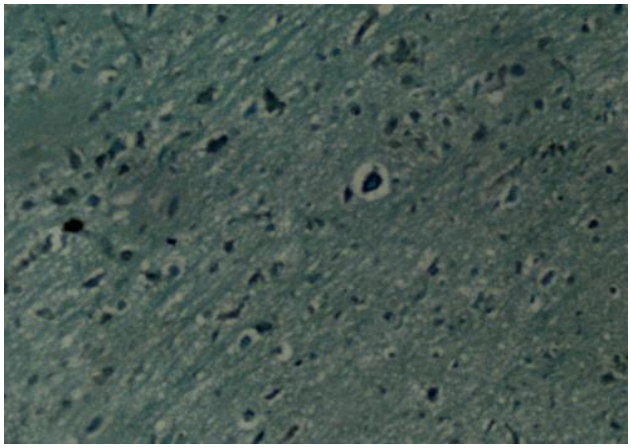
negative staining of the neurofibrillary tangle and senile plaques (BielschowskyX400). Figure 12

Figure 13: Group B (Silver Beilschowsky Stain).



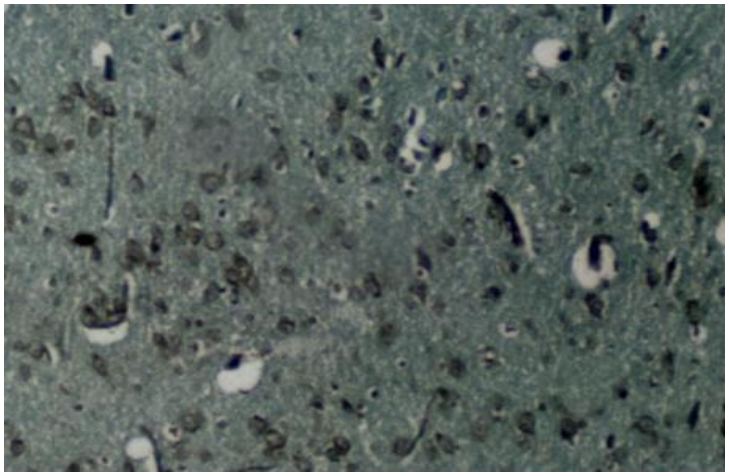
Group B (5mg/kg of HgCl2): A section of brain (Basal ganglion) section of albino rat shows negative staining of the neurofibrillary tangle and mild positive staining of the senile plaques (arrow) (Bielschowsky X400). Figure 13

Figure 14: Group C (Silver Beilschowsky Stain).



Group C (500 mg/kg of Ethanolic extract of aloe barbadensis): A section of brain (Basal ganglion) section of albino rat shows negative staining of the neurofibrillary tangle senile plaques (Bielschowsky X400). Figure 14

Figure 15: Group D (Silver Beilschowsky Stain).



Group D (5mg/kg of HgCl2 for 3-weeks + 250 mg/kg of Ethanolic extract of aloe barbadensis): A section of brain (Basal ganglion) section of albino rat shows negative staining of the neurofibrillary and Senile plaques (Bielschowsky X400). Figure 15

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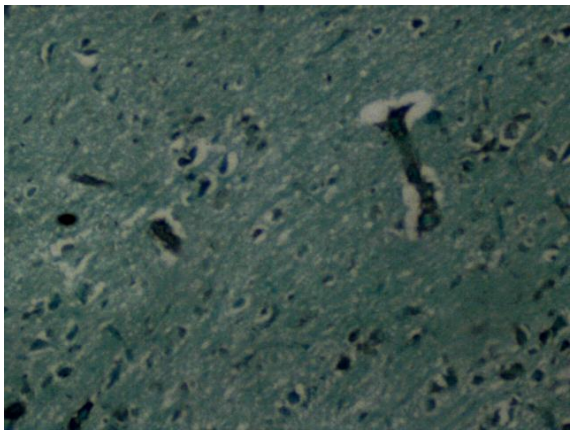
Figure 16: Group E (Silver Beilschowsky Stain).



Group E (5mg/kg of HgCl2 for 3-weeks + 500 mg/kg of Ethanolic extract of aloe barbadensis): A section of brain (Basal ganglion) section of albino rat showing negative staining of the neurofibrillary tangle and negative staining of the Senile plaques (BielschowskyX400). Figure 16

DISCUSSION

The primary objective of this research was to assess the ameliorative effects of ethanolic leaf extract from Aloe barbadensis (Aloe vera) against the neurotoxic impact of mercury chloride, which is known to provoke Alzheimer-like symptoms in the basal ganglia of albino Wistar rats. Mercury chloride, identified as a hazardous environmental pollutant, interferes with brain function by promoting oxidative stress and cellular damage ([17],[18]). Its neurotoxicity manifests through behavioral disturbances, biochemical disruptions, and structural degeneration that resemble Alzheimer's disease pathology[18]. Given the therapeutic promise of plant-based compounds, Aloe barbadensis, rich in antioxidants like aloin, aloe-emodin, and ace Mannan, was selected for its potential to counteract these effects ([20],[6]). This study explored its influence on anxiety and memory behavior, oxidative stress markers, neurotransmitter levels, and histological changes in brain tissue, aiming to establish its role as a natural intervention for mercury-induced neurodegeneration.

Neurobehavioral assessments evaluates motor, sensory, and cognitive function[11]. The neurobehavioral outcomes of this study offer compelling evidence of the impact of mercury chloride on brain function and the therapeutic potential of Aloe barbadensis in reversing these effects. Two behavioral paradigms—open field test and novel object recognition test—were employed to assess anxiety levels and recognition memory, respectively.Mercury chloride, a known neurotoxin, significantly elevated anxiety levels in rats, as evidenced by the open field test. Rats in Group B, which received mercury chloride alone, exhibited a marked increase in anxiety index compared to both the untreated control group and those treated with Aloe barbadensis. This behavioral alteration aligns with established literature indicating that mercury disrupts neurotransmitter systems and induces oxidative stress, particularly in brain regions responsible for emotional regulation ([17],[18]).

Interestingly, Group C, which received only Aloe barbadensis extract without mercury exposure, demonstrated a significant reduction in anxiety index relative to the control group. This suggests that the extract may possess intrinsic anxiolytic properties, potentially mediated by its rich phytochemical composition—including polysaccharides, flavonoids, and anthraquinones—which are known to modulate oxidative pathways and neuroinflammation ([6]; [16]). The anxiolytic-like effects observed in the Aloe-treated groups (D and E) further support the hypothesis that Aloe barbadensis can counteract mercury-induced emotional disturbances.

In the novel object recognition test, which assesses recognition memory, rats in Groups C, D, and E exhibited significantly higher recognition indices than both the control and mercury-only groups. This enhancement in memory performance suggests that Aloe barbadensis not only protects against cognitive deficits induced by mercury but may also enhance baseline cognitive function. These findings are consistent with previous studies that attribute memory-enhancing effects of Aloe-based formulations to their antioxidant and anti-inflammatory actions, which help preserve synaptic integrity and neurotransmitter balance ([25],[20]).

Notably, there was no significant difference in recognition index between the mercury-only group (Group B)

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and the control group (Group A), indicating that the duration or dosage of mercury exposure may have had a more pronounced effect on anxiety-related behavior than on recognition memory within the study's timeframe. Nevertheless, the cognitive improvements observed in the Aloe-treated groups reinforce the extract's neuroprotective potential. These results suggest that Aloe barbadensis may exert its effects by restoring redox balance, enhancing cholinergic function, and reducing neuronal damage—mechanisms that are crucial in the context of neurodegenerative conditions such as Alzheimer's disease ([24],[6]).

The biochemical results from this study highlight the oxidative stress and neurochemical disruptions caused by mercury chloride, as well as the restorative effects of Aloe barbadensis extract. Mercury chloride exposure led to a marked reduction in SOD activity in Group B, indicating weakened antioxidant defenses and heightened oxidative stress. This aligns with previous studies by [17] and [18], which reported that mercury compounds impair enzymatic antioxidant systems in the brain. In contrast, Groups C, D, and E—treated with Aloe barbadensis—showed significantly elevated SOD levels compared to both the control and mercury-only groups. This suggests that the extract enhances antioxidant enzyme activity, likely due to its bioactive compounds such as flavonoids and polysaccharides ([20], [6]).

MDA levels were significantly higher in Group B, confirming the presence of lipid peroxidation and oxidative damage. Although Groups C, D, and E showed reduced MDA levels compared to Group A, these differences were not statistically significant. However, the significant reduction in MDA levels compared to Group B indicates that Aloe barbadensis effectively counteracts mercury-induced oxidative stress, consistent with findings by [24] and [26], who demonstrated the extract's ability to protect neuronal membranes from oxidative injury.

AChE activity was notably reduced in Group B, reflecting impaired cholinergic transmission—a hallmark of Alzheimer-like neurodegeneration. Mercury's interference with neurotransmitter systems has been documented to affect memory and learning processes[18]. Groups D and E showed a significant increase in AChE activity compared to both Group A and Group B, while Group C showed an increase that was not statistically significant.

Rats in (Group B) exposured to mercury chloride showed a significant reduction in glutamate levels, indicating impaired excitatory neurotransmission and potential excitotoxic damage. This finding is consistent with previous research by [24] and [2], which demonstrated that mercury disrupts glutamate transport and contributes to neuronal dysfunction. In contrast, rats in (Groups C and D) treated with

Aloe barbadensis extract showed increased glutamate levels compared to the control group, suggesting that Aloe plays a role in restoring glutamatergic balance. This aligns with the findings of [3], who showed that Aloe exhibits neuroprotective effects against glutamate-induced toxicity. However, Group E, which received mercury and a high dose of Aloe, did not show significant improvement, possibly due to dose-dependent modulation or saturation of Aloe's effect. As noted by [6], higher concentrations of Aloe may have different effects on neurotransmitter dynamics, warranting further investigation. These results suggest that Aloe barbadensis may help restore cholinergic function, particularly when administered after mercury exposure. Its neuroprotective effect may be attributed to its ability to reduce oxidative stress and preserve neuronal integrity ([6],[16]).

Histological Observations

H&E Staining of the Basal Ganglia

The histological assessment of the basal ganglia using hematoxylin and eosin (H&E) staining revealed distinct cellular alterations across the experimental groups, offering valuable insight into the neurotoxic effects of mercury chloride and the restorative potential of Aloe barbadensis extract.

Group A (Control – Feed and Water ad libitum) - Tissue sections from the control group displayed well-preserved neural architecture. The basal ganglia, particularly the caudate and putamen regions, showed a dense population of medium-sized neurons with clearly defined nuclei. Surrounding these neurons were numerous glial cells, including astrocytes and oligodendrocytes, embedded within a richly textured neuropil composed of dendrites, axons, and synaptic terminals. This intact histological profile reflects a healthy and functional neural environment, consistent with normal striatal morphology described in neuroanatomical literature [13].

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Group B (Mercury Chloride – 5 mg/kg)**-** Sections from rats exposed to mercury chloride revealed significant histopathological alterations. There was a moderate reduction in neuronal and glial cell populations, accompanied by the presence of pyknotic nuclei—indicative of chromatin condensation and early neuronal death. These changes are characteristic of mercury-induced neurotoxicity, which disrupts mitochondrial function and promotes oxidative stress, leading to apoptosis and neuroinflammation [24]. The damage observed in the basal ganglia underscores mercury's affinity for sulfhydryl groups in neuronal proteins, impairing cellular metabolism and structural integrity.

Group C (Aloe barbadensis Extract – 500 mg/kg) -Histological sections from rats treated with Aloe barbadensis extract alone showed a robust population of large, healthy neurons and glial cells. The preservation of cellular architecture suggests that the extract may enhance neuronal resilience or support neurogenesis. These effects are likely mediated by the plant's bioactive compounds—such as aloin, aloe-emodin, and acemannan—which possess antioxidant and anti-inflammatory properties that stabilize neural membranes and reduce oxidative burden [6].

In group D (Mercury + Aloe barbadensis – 250 mg/kg), the basal ganglia exhibited moderate neuronal and glial cell loss. While the damage was less severe than in the mercury-only group, it was still evident, indicating partial neuroprotection. The reduced efficacy at this lower dose suggests a dose-dependent relationship between Aloe barbadensis administration and its neuroprotective capacity. This finding aligns with previous studies showing that higher concentrations of plant-derived antioxidants are more effective in counteracting heavy metal-induced neuronal damage [13].

Group E (Mercury + Aloe barbadensis – 500 mg/kg) **-** Sections from this group revealed normal neuronal and glial populations, suggesting a more substantial protective effect than observed in Group D. The improved histological profile supports the hypothesis that higher doses of Aloe barbadensis offer enhanced neuroprotection, likely through increased antioxidant enzyme activity and reduced lipid peroxidation. These findings are consistent with [24] and [6], who reported that plant-based antioxidants can significantly mitigate mercury-induced neurodegeneration when administered at therapeutic levels.

The H&E staining results clearly demonstrate the neurotoxic impact of mercury chloride on the basal ganglia, characterized by neuronal shrinkage, pyknotic nuclei, and glial cell loss. Treatment with Aloe barbadensis extract, particularly at 500 mg/kg, showed substantial histological improvement, reinforcing its role as a neuroprotective agent. These findings are consistent with literature highlighting the extract's antioxidant, anti-inflammatoryand neurorestorative properties, making it a promising plant for mitigating heavy metal-induced neurodegeneration.

Silver Bielschowsky Staining of the Basal Ganglia

Silver Bielschowsky staining is a specialized technique used to detect hallmark features of neurodegeneration, particularly neurofibrillary tangles (NFTs) and senile plaques—both of which are closely associated with Alzheimer's disease pathology. The staining patterns observed across the experimental groups in this study provide valuable insight into the extent of mercury-induced damage and the neuroprotective effects of Aloe barbadensis Miller.

Group A (Control) -Brain sections from the control group revealed negative staining for neurofibrillary tangles and no evidence of senile plaque formation. The absence of sparse tangles and plaques indicates preserved neural integrity in the basal ganglia [13].

Group B (Mercury Chloride Only) -Sections from rats exposed to mercury chloride showed a reversal in staining pattern—no detectable neurofibrillary tangles but mild positive staining for senile plaques. This indicates that mercury exposure may accelerate amyloid plaque formation while disrupting tau protein aggregation pathways. Mercury's neurotoxicity is known to promote oxidative stress and protein misfolding, contributing to the deposition of amyloid material in brain regions critical for cognition and motor control ([24],[18]).

In rats treated with Aloe barbadensis extract alone, both neurofibrillary tangles and senile plaques were absent. This clean histological profile suggests that the extract may prevent age-related neurodegenerative changes and

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maintain neuronal health. The absence of pathological markers supports the extract's antioxidant and anti-inflammatory properties, which help preserve protein stability and prevent oxidative damage [6].

Group D (Mercury + 250 mg/kg Aloe barbadensis) -Sections from this group also showed no staining for either neurofibrillary tangles or senile plaques, indicating that even a moderate dose of Aloe barbadensis was effective in preventing mercury-induced neurodegeneration. This suggests that the extract may inhibit both amyloid deposition and tau pathology, possibly by enhancing antioxidant defenses and modulating inflammatory responses [20].

In group E, negative staining for neurofibrillary tangles and senile plaques was observed. Compared to group B, this pattern reflects complete protection, with the higher dose of Aloe barbadensis effectively suppressing plaque formation. This outcome supports the dose-dependent efficacy of the extract and its ability to reduceneurofibrillary pathology under toxic conditions [25].

The Silver Bielschowsky staining results demonstrate that mercury chloride promotes senile plaque formation in the basal ganglia, while Aloe barbadensis extract—especially at higher doses—can effectively prevent or reduce these neurodegenerative markers. These findings reinforce the therapeutic potential of Aloe barbadensis in protecting against heavy metal-induced brain damage and Alzheimer-like pathology.

The outcomes of this study reaffirm the well-documented neurotoxic effects of mercury chloride, which include oxidative stress, neurotransmitter disruption, and structural damage to brain tissue. Behavioral deficits, biochemical imbalances, and histological abnormalities observed in mercury-treated rats align with previous research showing that mercury exposure leads to neuronal death, lipid peroxidation, and glial cell depletion—particularly in the basal ganglia, a region vital for motor coordination and cognitive processing ([24],[18]). The behavioral impairments observed in mercury-exposed rats, including heightened anxiety and diminished recognition memory, reflect symptoms commonly seen in the early stages of Alzheimer's disease. These deficits are associated with disruptions in neurotransmitter systems, particularly the cholinergic pathways, alongside increases in oxidative stress indicators such as malondialdehyde (MDA). Histological evidence of senile plaques further substantiates the pathological similarity to Alzheimer's disease [9].

Remarkably, administration of Aloe barbadensis extract significantly counteracted these adverse effects. Treated rats demonstrated reduced anxiety, enhanced memory performance, increased levels of superoxide dismutase (SOD), lowered malondialdehyde (MDA), and normalized acetylcholinesterase (AChE) activity. These improvements suggest that Aloe barbadensis confers neuroprotection through its diverse phytochemicals—such as acemannan, which boosts immune response and scavenges free radicals, b**eta-sitosterol** which binds acetylcholinesterase and butyrylcholinesterase, improving cholinergic function[10], aloinand aloe-emodin, which inhibits lipid peroxidation and reduce neuroinflammation. These phytochemicals are known to neutralize free radicals, regulate inflammatory responses, and promote neuronal survival ([7],[3]).

Histological evaluations using H&E and Silver Bielschowsky staining further validated the extract's protective role. Mercury exposure resulted in pyknotic nuclei, reduced neuronal density, and mild plaque formation—features reminiscent of Alzheimer's disease. In contrast, rats treated with Aloe barbadensis showed preserved brain architecture and minimal or absent neurofibrillary tangles and senile plaques. These findings are consistent with studies indicating that plant-derived antioxidants can suppress amyloid plaque formation and tau protein hyperphosphorylation—two key pathological processes in Alzheimer's progression ([9],[20]).

Emerging research also suggests that compounds in Aloe barbadensis may exert their effects by modulating multiple neuroprotective pathways, including ApoE4/LRP1, Wnt/β-catenin, and TLR4/NLRP3 signaling. These pathways are involved in neuroinflammation, synaptic regulation, and amyloid clearance, further supporting Aloe's potential as a multi-targeted therapeutic agent for neurodegenerative conditions [9].

In broader context, reviews of medicinal plants in Alzheimer's therapy highlight Aloe barbadensis as a promising herb for reducing oxidative damage and preserving cognitive function. Reference[21] emphasized Aloe's role in enhancing synaptic plasticity and mitigating neuroinflammation, while [4] advocated for the integration of African phytochemicals like Aloe into Alzheimer's treatment strategies due to their accessibility, affordability, and diverse mechanisms of action.

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CONCLUSIONS

This study provides compelling evidence that the ethanolic extract of Aloe barbadensis effectively mitigates mercury-induced Alzheimer-like alterations in the basal ganglia of Wistar rats. Across behavioral, biochemical, and histological domains, the extract demonstrated a robust capacity to reverse neurotoxic damage—reducing anxiety, enhancing memory, restoring antioxidant enzyme activity, and preserving neuronal integrity.

The significance of these findings lies in the extract's ability to counteract hallmark features of neurodegeneration, including oxidative stress, cholinergic dysfunction, and the formation of senile plaques and neurofibrillary tangles. These pathological markers are central to Alzheimer's disease, and their attenuation by Aloe barbadensis suggests that the plant's bioactive compounds—such as acemannan, aloinand aloe-emodin—may modulate key neuroprotective pathways.

Given its accessibility, affordability, and multi-targeted therapeutic potential, Aloe barbadensis emerges as a promising natural agent for managing heavy metal-induced neurotoxicity and Alzheimer-like symptoms. Its integration into preventive or adjunctive strategies could offer a safer, plant-based alternative in the broader context of neurodegenerative disease management.

Suggestions for Further Research

While this study highlights the neuroprotective potential of Aloe barbadensis against mercury-induced damage, further research is warranted to deepen our understanding of its therapeutic mechanisms. Future studies should:

- Investigate the molecular pathways involved in Aloe's antioxidant and anti-inflammatory effects, including its influence on tau phosphorylation, amyloid clearance, and neuroinflammatory signaling.
- Explore dose-response relationships and long-term safety profiles to determine optimal therapeutic windows.
- Conduct clinical trials to assess its efficacy in human populations, particularly in individuals at risk for heavy metal exposure or neurodegenerative conditions like Alzheimer's disease.
- Utilize advanced techniques such as gene expression profiling, proteomics and immunohistochemistry to validate its effects at the cellular and molecular levels.

These directions will help translate the promising results of this study into practical applications for neuroprotective therapy.

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REFERENCES

1. Al-Attar, A. M., and Abu Zeid, I. M. (2013). Effect of tea (camellia sinensis) and olive (olea europaea L.) leaves extracts on male mice exposed to diazinon. BioMed Research International, 2013, 1–6. https://doi.org/10.1155/2013/461415
2. Albrecht, J., & Matyja, E. (1996). Metabolic Brain Disease, 11(3), 175–184. https://doi.org/10.1007/BF02069504
3. Bamigboye, S. O. et al. (2020). Neuroprotective effects of aqueous extract of Aloe barbadensis on cortical cells. Nigerian Journal of Natural Products and Medicine, 23(1). https://www.ajol.info/index.php/njnpm/article/view/195768
4. Ben-Azu, B., Oghorodi, A. M., Oritsemuelebi, B., & Chidebe, E. O. (2024). A case for the neuroprotective potential of African phytochemicals in the management of Alzheimer's disease. In Cognitive Human Neuroscience – From Assessment to Neuroprotection. IntechOpen. https://www.intechopen.com/chapters/89142
5. Chamoli, A., and Karn, S. K. (2024). The Effects of Mercury Exposure on Neurological and Cognitive Dysfunction in Human: A Review. In N. Kumar (Ed.), Mercury Toxicity Mitigation: Sustainable Nexus Approach (pp. 117–135). Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-48817-7_5

6. Enogieru, A. B., Hayatudeen, N., & Omotoso, G. O. (2023). Protective effects of Aloe barbadensis against mercury-induced neurotoxicity in rats. Journal of Phytomedicine and Therapeutics, 22(1), 45–56. https://www.ajol.info/index.php/jopat/article/view/284522
7. Enogieru, A., and Omoruyi, S. (2022). Exploration of Aqueous Phyllanthus amarus Leaf Extract as a Protective Agent in Mercury Chloride-Exposed Wistar Rats: A Neurobehavioural Study. Journal of Applied Sciences and Environmental Management, 26, 629–637. https://doi.org/10.4314/jasem.v26i4.10
8. Españo, E., Kim, J., and Kim, J.-K. (2022). Utilization of Aloe Compounds in Combatting Viral Diseases. In Pharmaceuticals (Vol. 15, Issue 5, p. 599). https://doi.org/10.3390/ph15050599
9. Hamdan, A. M. E., Alharthi, F. H. J., Alanazi, A. H., & El-Emam, S. Z. (2022). Neuroprotective effects of phytochemicals against aluminum chloride-induced Alzheimer's disease through ApoE4/LRP1, Wnt3/β-Catenin/GSK3β, and TLR4/NLRP3 pathways. Pharmaceuticals, 15(8), 1008. https://doi.org/10.3390/ph15081008
10. Khedraoui, M. et al. (2025). Aloe vera compounds show promise in Alzheimer's disease treatment. https://www.eurekalert.org/news-releases/1100055
11. Kim, Y., and Kim, J. W. (2012). Toxic Encephalopathy. Safety and Health at Work, 3(4), 243–256. https://doi.org/https://doi.org/10.5491/SHAW.2012.3.4.243
12. Korczyn, A. D., and Grinberg, L. T. (2024). Is Alzheimer disease a disease? Nature Reviews Neurology, 20(4), 245–251. https://doi.org/10.1038/s41582-024-00940-4
13. Kumari, K., & Chand, G. B. (2023). Effects of mercury: Neurological and cellular perspective. In Environmental Science and Engineering (pp. 141–162). Springer. https://link.springer.com/chapter/10.1007/978-981-99-7719-2_5
14. Maan, A. A., Nazir, A., Khan, M. K. I., Ahmad, T., Zia, R., Murid, M., and Abrar, M. (2018). The therapeutic properties and applications of Aloe vera: A review. Journal of Herbal Medicine, 12, 1-10. https://doi.org/10.1016/j.hermed.2018.01.002
15. Mair, R. G., Francoeur, M. J., Krell, E. M., and Gibson, B. M. (2022). Where Actions Meet Outcomes: Medial Prefrontal Cortex, Central Thalamus, and the Basal Ganglia. Frontiers in Behavioral Neuroscience, 16, 928610. https://www.frontiersin.org/journals/behavioralneuroscience/articles/10.3389/fnbeh.2022.928610
16. Matei, A., Popescu, M., & Ionescu, A. (2025). Phytochemical modulation of neuroinflammation: Therapeutic prospects of Aloe barbadensis. Neurobiology of Disease, 185, 106045. https://doi.org/10.1016/j.nbd.2025.106045
17. Mesquita, M., Pedroso, T. F., Oliveira, C. S., Oliveira, V. A., Do Santos, R. F., Bizzi, C. A., and Pereira, M. E. (2016). Effects of zinc against mercury toxicity in female rats 12 and 48 hours after HgCl2exposure. EXCLI Journal, 15(valence 0), 256–267. https://doi.org/10.17179/excli2015-709
18. Nabil, A., Elshemy, M. M., Asem, M., and Gomaa, H. F. (2020). Protective Effect of DPPD on Mercury Chloride-Induced Hepatorenal Toxicity in Rats. Journal of Toxicology, 2020, 1–7. https://doi.org/10.1155/2020/4127284
19. Nwozo, O. S., Effiong, E. M., Aja, P. M., and Awuchi, C. G. (2023). Antioxidant, phytochemical, and therapeutic properties of medicinal plants: a review. International Journal of Food Properties, 26(1), 359–388. https://doi.org/10.1080/10942912.2022.2157425
20. Pammi, S. S. S., Suresh, B., and Giri, A. (2023). Antioxidant potential of medicinal plants. Journal of Crop Science and Biotechnology, 26(1), 13–26. https://doi.org/10.1007/s12892-022-00159-z
21. Prajwal, S., & Kumar, M. R. (2022). The neuroprotective effects of medicinal plants on Alzheimer's disease: A review. Asian Journal of Advances in Medical Science, 4(1), 135–146. https://journalmedicals.com/index.php/AJOAIMS/article/view/110
22. Sánchez, M., González-Burgos, E., Iglesias, I., and Gómez-Serranillos, M. P. (2020). Pharmacological Update Properties of Aloe Vera and its Major Active Constituents. In Molecules (Vol. 25, Issue 6, p. 1324). https://doi.org/10.3390/molecules25061324
23. Silva, M. V. F., Loures, C. de M. G., Alves, L. C. V., de Souza, L. C., Borges, K. B. G., and Carvalho, M. das G. (2019). Alzheimer's disease: risk factors and potentially protective measures. Journal of Biomedical Science, 26(1), 33. https://doi.org/10.1186/s12929-019-0524-y
24. Teixeira, F. B., de Oliveira, A. C. A., Leão, L. K. R., Fagundes, N. C. F., Fernandes, R. M., Fernandes, L. M. P., da Silva, M. C. F., Amado, L. L., Sagica, F. E. S., de Oliveira, E. H. C., Crespo-Lopez, M. E., Maia, C. S. F., and Lima, R. R. (2018). Exposure to Inorganic Mercury Causes Oxidative Stress, Cell Death, and Functional Deficits in the Motor Cortex. In Frontiers in Molecular Neuroscience (Vol. 11, p. 337445). https://www.frontiersin.org/articles/10.3389/fnmol.2018.00125

25. Velázquez-López, L., Martínez-González, C. L., & Ramírez-Moreno, E. (2023). Neuroprotective effects of Aloe vera on oxidative stress and memory impairment: A review. Journal of Ethnopharmacology, 310, 116295. https://doi.org/10.1016/j.jep.2023.116295
26. Yılmaz, A., et al. (2021). Journal of Anatolian Environmental and Animal Sciences, 6(3), 376–381. https://doi.org/10.35229/jaes.953830
27. Yu, P. H., Wright, S., Fan, E. H., Lun, Z. R., and Gubisne-Harberle, D. (2003). Physiological and pathological implications of semicarbazide-sensitive amine oxidase.