Review Article

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Impact of Aluminium Chloride ($AlCl_3$) on Brain Function: A Review of Neurotoxic Mechanisms and Implications for Alzheimer's Disease

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Abstract

Aluminium chloride ($AlCl_3$) is a prevalent environmental pollutant found in food and drinking water. Epidemiological studies suggest a strong link between $AlCl_3$ exposure and neurodegenerative disorders, especially Alzheimer's disease (AD). $AlCl_3$ disrupts normal brain function, potentially leading to oxidative stress, inflammatory responses, and cognitive decline, all of which are implicated in AD pathology. This review compiled and analysed data from 59 studies, accessed through academic databases such as Google Scholar, PubMed, Springer, Science Direct, Wiley, Scopus, and Research Gate. The focus was specifically on the neurotoxic effects of $AlCl_3$, drawing insights into its impact on brain structure, function, and behaviour. Findings from the reviewed studies reveal that $AlCl_3$ exposure leads to increased aluminium accumulation in brain tissues, resulting in structural damage and neurotoxic effects. This accumulation affects cognitive functions and behaviour, with histological analyses showing signs of neurodegeneration. Behavioural changes and impaired cognitive abilities observed in animal and cellular models suggest that $AlCl_3$ disrupts neural pathways critical to learning and memory. The evidence indicates a significant association between $AlCl_3$ exposure and neurodegenerative damage, especially in the context of AD. This review emphasizes the need for further research into $AlCl_3$'s neurotoxic mechanisms to clarify its role in AD and other neurodegenerative diseases. Enhanced understanding may help develop preventive measures and regulations to mitigate the health risks posed by aluminium exposure in daily life.

Keywords: Aluminium chloride, Alzheimer's disease, Neurotoxicity, Oxidative stress, Cognitive impairment.

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1. Introduction

Aluminium chloride ($AlCl_3$) is recognized as a neurotoxicant that disrupts brain structure and function, particularly by irritating the hippocampus and impairing neurogenesis. Aluminium, a common element in the Earth's crust, is released into the environment through natural geological processes and human activities, including mining and industrial operations. Although the direct use of aluminium compounds is relatively limited, they are employed in various applications such as water treatment, paper manufacturing, fire retardants, fillers, food additives, colorants, and medicines (1).For the general population, the primary source of aluminium intake is through food. Common dietary sources include bread, cakes, sweet pastries, glacé fruits, dairy products, sausages, shellfish, sugar-containing

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foods, and baking powder. Additionally, aluminium concentrations are notably high in tea leaves, herbs, cocoa, cocoa products, and spices. Research indicates that, under typical conditions, the release of aluminium from food contact materials (FCMs) can lead to increased dietary intake of aluminium. While aluminium-containing antacids and buffered aspirin are generally considered safe when used at recommended doses, concerns persist about their long-term effects (1). The first pioneering investigations into aluminium neurotoxicity were reported in 1886 by Siem and Dollken (2). Significant insights into aluminium toxicity in humans have emerged from studies involving patients exposed to dialysis solutions containing aluminium concentrations at or above 0.5 mmol/L. In these patients, aluminium deposition was observed in various tissues, including the kidneys, liver, bones, and brain, leading to pathological conditions such as dementia, osteomalacia, and osteodystrophy. The primary transporter of aluminium in plasma is transferrin, an iron-binding protein that facilitates the entry of aluminium into the brain and placenta, thereby posing risks to neurological development and function (1). This review aims to evaluate the neurotoxic effects of aluminium chloride ($AlCl_3$) on brain structure and function, particularly its impact on the hippocampus and neurogenesis. It also explores key sources and pathways of human aluminium exposure, focusing on health risks associated with long-term exposure.

2. Aluminium chloride and oxidative stress

Aluminium chloride ($AlCl_3$) is recognized for its neurotoxic effects, particularly its role in inducing oxidative stress. Oxidative stress arises when there is an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them, leading to cellular damage. This phenomenon plays a significant role in the pathogenesis of several diseases, especially neurodegenerative disorders. $AlCl_3$ exposure is known to disrupt antioxidant defences, causing lipid peroxidation and damage to critical cellular components in various organs, with a significant impact on the brain.

2.1. Mechanisms of oxidative stress induced by $AlCl_3$

2.1.2. Generation of reactive oxygen species (ROS)

Exposure to $AlCl_3$ significantly increases the production of ROS. These highly reactive molecules contribute to oxidative damage by attacking cellular lipids, proteins, and DNA. ROS promote the formation of toxic products like malondialdehyde (MDA), a marker of lipid peroxidation, and are implicated in cellular dysfunction. In addition, ROS cause a reduction in the activity of antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), leading to further cellular injury (3-6).

2.1.2. Damage to cellular components

The elevated ROS levels resulting from $AlCl_3$ exposure lead to widespread cellular damage. This includes increased levels of protein carbonyls, lipid peroxidation, and DNA damage, which are indicative of oxidative stress-induced cellular injury. $AlCl_3$ induces alterations in neuronal cells by disrupting their membranes and DNA structure. Furthermore, the Fenton reaction, facilitated by aluminium ions, converts hydrogen peroxide into highly reactive hydroxyl radicals, exacerbating oxidative damage (5, 6).

2.1.3. Inhibition of antioxidant activities

Antioxidant enzymes, such as SOD, CAT, and GSH, are crucial in maintaining cellular redox balance by scavenging ROS. $AlCl_3$ exposure has been shown to inhibit the activity of these enzymes, resulting in a weakened defence against oxidative damage. The depletion of these protective enzymes leads to an accumulation of ROS, further exacerbating the cellular stress and damage.

2.2. Neurotoxicity and cognitive impairment

$AlCl_3$ has been studied for its neurotoxic effects, particularly regarding its potential to induce cognitive deficits and neurodegenerative changes that mimic Alzheimer's disease. The oxidative stress generated by $AlCl_3$ contributes to neuronal damage, leading to dysfunction in brain cells. Chronic exposure to $AlCl_3$ has been shown to impair learning and memory functions in animal models, a consequence of oxidative damage to the brain's antioxidant defence system. The neurotoxic effects of $AlCl_3$ are mediated through oxidative stress, which disrupts the integrity and function of neuronal cells (7, 8).

2.3. Oxidative stress and lipid peroxidation

2.3.1. Lipid peroxidation

Lipid peroxidation refers to the oxidative degradation of lipids, leading to the formation of toxic products like MDA. MDA is considered a reliable marker of lipid damage and oxidative stress. $AlCl_3$ exposure has been shown to significantly increase MDA levels, indicating severe lipid damage within cells. The accumulation of MDA is associated with the disruption of cellular membranes, impairing cellular function. In addition to being a marker of oxidative stress, MDA is implicated in the pathophysiology of several diseases, including cancer and neurodegenerative disorders (9-11).

2.3.2. Superoxide dismutase (SOD)

Superoxide dismutase (SOD) is an essential antioxidant enzyme responsible for converting superoxide radicals into hydrogen peroxide and oxygen. SOD plays a key role in protecting cells from oxidative damage. However, exposure to $AlCl_3$ has been shown to decrease SOD activity, which impairs the body's ability to neutralize harmful free radicals. This reduction in SOD activity contributes to the increased oxidative burden on cells, leading to further damage and dysfunction (10-12).

2.3.3. Reduced glutathione (GSH)

Glutathione (GSH) is a vital antioxidant that plays a central role in protecting cells from oxidative damage. GSH acts as a reducing agent that detoxifies ROS and maintains cellular redox balance. $AlCl_3$ exposure leads to a decrease in GSH levels, which weakens the cellular antioxidant defense system and promotes the accumulation of ROS. The depletion of GSH is associated with increased MDA production, indicating the progression of lipid peroxidation and oxidative damage (9-13).

3. Effects of Aluminium chloride on the cerebral cortex: Histological evaluations

The administration of Aluminium Chloride ($AlCl_3$) in experimental models, such as Wistar rats, has been linked to various significant histopathological changes in the cerebral cortex. These changes reflect the neurotoxic effects of aluminium exposure and are highlighted by several key features:

3.1. Necrosis

Histopathological studies reveal the occurrence of necrosis within the cortical layers of the brain following Aluminium chloride exposure. Necrosis is characterized by the death of neurons and surrounding tissues, which disrupts the structural integrity of the cerebral cortex. This effect is notably pronounced, with Aluminium acting as a potent toxin, leading to irreversible cellular damage (14-18).

3.2. Cytoplasmic vacuolations

Another significant histological alteration is the formation of vacuoles within the cytoplasm of neuronal cells. These vacuoles are indicative of cellular stress or damage and interfere with the normal function of the neuron. The presence of vacuoles suggests that Aluminium exposure is contributing to cellular dysfunction, potentially leading to neuronal degeneration (14).

3.3. Karyopyknosis

Karyopyknosis refers to the condensa-

tion of chromatin within the nucleus, a hallmark of apoptosis. The presence of karyopyknosis in neurons exposed to Aluminium chloride suggests an ongoing apoptotic process, which supports the notion of aluminium-induced neurotoxicity. This nuclear alteration is associated with neuronal loss and contributes to the progression of neurological impairments (14).

3.4. Oxidative stress

Aluminium exposure has been shown to disrupt oxidative balance in the brain. Increased levels of malondialdehyde (MDA), a marker of lipid peroxidation, and decreased activity of superoxide dismutase (SOD), an antioxidant enzyme, indicate elevated oxidative stress. This imbalance results in cellular damage, including lesions in the cortex and hippocampus, and impairs neuronal function. The oxidative damage exacerbates neurodegeneration, contributing to cognitive deficits (15, 16).

3.5. Neuroinflammation

Chronic exposure to Aluminium chloride also triggers inflammatory responses within the brain, a process known as neuroinflammation. This inflammation can exacerbate neuronal damage, leading to further cognitive dysfunction. The neuroinflammatory response is a significant factor in the development of neurodegenerative conditions such as Alzheimer's disease (17, 18).

4. Role of cellular organelles in aluminium chloride neurotoxicity

Aluminium's neurotoxic effects are closely linked to its impact on various cellular organelles. These organelles play essential roles in cellular metabolism, protein synthesis, and cellular integrity. Aluminium's interference with their functions leads to neuronal damage and dysfunction.

4.1. Mitochondria

Mitochondria are critical for energy production and cellular metabolism. Aluminium accumulation in mitochondria disrupts ATP synthesis and enhances oxidative stress, leading to mitochondrial injury. This damage is associated with increased levels of reactive oxygen species (ROS) and decreased antioxidant capacity, further exacerbating cellular injury. Mitochondrial dysfunction is a key feature in the pathogenesis of neurodegenerative diseases (19).

4.2. Nucleus

The nucleus, which houses the cell's genetic material, is particularly vulnerable to the toxic effects of aluminium. Studies have shown that aluminium exposure induces genotoxicity, including DNA fragmentation and chromosomal abnormalities. Aluminium impedes the DNA damage response by downregulating critical genes like BRCA1 and BRCA2, which are involved in DNA repair. This impairment leads to increased mutation rates and a higher risk of cancer and cognitive decline (19-21).

4.3. Endoplasmic reticulum (ER)

The endoplasmic reticulum (ER) plays a crucial role in protein synthesis and folding. Aluminium exposure triggers ER stress, which activates the unfolded protein response (UPR). Chronic ER stress can lead to neuronal apoptosis and neurodegenerative diseases. The accumulation of misfolded proteins, caused by aluminium-induced ER dysfunction, impairs cellular function and contributes to neuronal death (20).

4.4. Lysosomes

Lysosomes are responsible for the degradation of cellular waste and damaged organelles. Aluminium exposure can impair lysosomal function, disrupting the process of autophagy. This dysfunction leads to the accumulation of damaged proteins and organelles, promoting neuroinflammation and neuronal cell death. The resulting neurotoxic effects contribute to the progression of neurodegen-

erative diseases (22).

5. Aluminium chloride-induced alterations at genetic level

Aluminium chloride ($AlCl_3$) has been implicated in altering various genetic pathways within the brain. These alterations can lead to significant changes in cellular processes, influencing the progression of neurodegenerative diseases and other neurological conditions. This section outlines the genetic changes caused by $AlCl_3$ exposure, focusing on genes that regulate the cell cycle and oxidative stress responses, which are crucial in maintaining normal neuronal function.

5.1. Cell cycle control

Cyclin D1: Cyclin D1 plays a key role in regulating the cell cycle, particularly in the transition from G1 to S phase. $AlCl_3$ exposure has been shown to stimulate the expression of cyclin D1, which suggests that aluminium may influence cell cycle progression and potentially promote cell proliferation. This raises concerns about its role in cellular abnormalities within the brain (23).

5.2. p21 expression

p21 is a cyclin-dependent kinase inhibitor that controls the progression of the cell cycle by halting it at the G1 phase. $AlCl_3$ has been shown to induce the expression of p21, which serves as a protective mechanism against cellular damage. However, the simultaneous activation and inhibition of the cell cycle by aluminium present a complex scenario in cellular response to toxic exposure (23).

5.3. Genes assisting in oxidative stress inducement

Nrf2: Nrf2 is a master regulator of antioxidant defense mechanisms. When exposed to $AlCl_3$, the Nrf2 pathway is downregulated, which diminishes the cell's ability to counteract oxidative stress. This reduction contributes to cellular damage, potentially leading to neurodegenerative conditions (23).

5.4. Other genes

Cdk5 (Cyclin-dependent kinase 5): Cdk5 is a crucial regulator of neuronal differentiation and function. $AlCl_3$ exposure has been found to increase the expression of Cdk5, which may contribute to neurodegenerative processes by altering normal neuronal signaling and function (23).

Acetylcholinesterase (AChE): $AlCl_3$ affects the expression of AChE, an enzyme important for neurotransmission. This alteration may disrupt cholinergic signaling pathways, impacting cognitive functions such as memory and learning (24).

6. Mechanisms of action of aluminium chloride neurotoxicity

Aluminium chloride ($AlCl_3$) exerts its neurotoxic effects through several mechanisms that disrupt neuronal structure and function, significantly contributing to neurodegenerative diseases. Understanding these mechanisms is essential for exploring the broader implications of aluminium toxicity in the brain (Table 1).

6.1. Blood-brain barrier disruption

$AlCl_3$ can compromise the permeability of the BBB, allowing aluminium to accumulate within the brain. This accumulation is associated with the onset of several neurodegenerative diseases, including Alzheimer's disease (25-27).

6.2. Oxidative stress

$AlCl_3$ induces oxidative stress, which leads to neuronal damage. It reduces the activity of antioxidant enzymes and increases the levels of reactive oxygen species (ROS), causing cellular injury and apoptosis in brain tissue (28).

6.3. Neuroinflammation

$AlCl_3$ exposure results in neuroinflammation, which consistently exacerbates neurodegenerative changes in the brain. Elevated

Table 1. Aluminium Chloride Induced Neurotoxicity.

Animal model	Method of administration	Dose	Duration	Observation	Ref
Male Albino Wistar rats	Orally	17 mg/kg	21 days	In the $AlCl_3$-treated group, there were signs of blood cell leakage, immune cell infiltration, neuronal damage, increased liver enzymes, and swelling of blood vessels.	35
Sprague Dawley rats	Orally	17 mg/kg	28 days	The $AlCl_3$ group showed marked perineural and perivascular edema	36
Male Albino Wistar rats	Orally	50 mg/kg	28 days	The study investigated significant changes caused by $AlCl_3$ in the hippocampus, including increased deposits of eosinophilic plaques and β-amyloid plaques.	37
Male Albino Wistar rats	Orally	100 mg/kg	21 days	A significantly higher caspase 3 level was observed in $AlCl_3$ group	38
Albino Wistar rats	Orally	100 mg/kg	21 days	Histology examination of the aluminium control group indicated the presence of gross histopathological changes such as neurodegeneration, and animals had vacuolated cytoplasm	39
Sprague Dawley rats	Orally	100 mg/kg	28 days	The $AlCl_3$-treated group showed minor brain swelling and inflammation, but extensive damage including cell loss and the formation of scar tissue.	40
Sprague Dawley rats	Orally	100 mg/kg	36 days	Animals treated with $AlCl_3$ exhibited various types of degenerating neurons in the dentate gyrus and Cornu Ammonis regions, along with increased microglial cell presence and areas of reduced cell density.	32
Albino Wistar rats	Orally	150 mg/kg	90 days	he biochemical and neurochemical alterations induced by $AlCl_3$ are associated with a decline in cognitive capacity. This means that the changes in brain chemistry and cellular processes due to $AlCl_3$ exposure contribute to impaired cognitive abilities, such as memory and learning.	21
Albino Wistar rats	Orally	175mg/kg	60days	In the aluminium-treated group, numerous blackened, shrunken, and degenerating neurons were observed in the cerebral cortex, accompanied by neuronophagia (destruction of neurons) and gliosis (glial cell proliferation).	41
Male Albino Wistar rats	Orally	200mg/kg	14days	$AlCl_3$ group showed extensive neuronal degeneration	30
ICR mice	Orally	200mg/kg	8 weeks	In the CA1 and CA3 regions of the hippocampus in mice treated with Dgal/$AlCl_3$, there were low levels of Bcl-2 and high levels of Bax, Caspase 3, and Cyt-c. These findings indicate increased apoptosis or cell death in the hippocampus.	42
Albino Wistar rats	Orally	300mg/kg	60days	Long-term $AlCl_3$ treatment led to a significant increase in pyknotic neurons in the CA1 and CA3 regions, a decrease in mature pyramidal cells, and disorientation of the PVBL (parvalbumin-positive basket cells) in both regions. These changes suggest significant damage to hippocampal structure and function, which may contribute to cognitive impairments.	43

Continued Table 1.

Albino Wistar rats	I.P	10 mg/kg	60 days	Aluminium treatment caused severe damage in the rat hippocampus, including cell death, distorted neuron shapes, and altered nuclear structures, leading to significant neurological impairment.	44
Albino Wistar rats	I.P	32.5 mg/kg	60days	The histopathological changes of this particular area of the brain indicated pyramidal neurons that exhibited shrinkage of nuclei, swelling, vacuolation, as well as apoptotic cells upon $AlCl_3$ intoxication in the long term	45
Sprague-Dawley rats	I.P	50 mg/kg	28 days	Deposition of amyloid neurofibrillary tangles and swelling of pyramidal cells in $AlCl_3$-treated animals.	46
Male Albino Wistar rats	I.P	80 mg/kg	60days	Morphometric analysis depicted that in comparison to control; Al induced a highly significant increase in the number of dark cells p<0. 0001 in the Al group	47
Albino Wistar rats	I.P	100 mg/kg	60 days	Treatment with $AlCl_3$ significantly enhanced the immunostaining of amyloid precursor protein (APP) in the hippocampus and cortex of rats. This suggests an increased expression or accumulation of APP, which may impact amyloid-beta plaque formation and related neurodegenerative processes.	48
Adult male Sprague Dawley rats	Subcutaneous	10mg/kg	98days	It proved that the neurons in the cortex and hippocampus of AD groups are having nuclear loss and reduced size, cellular atrophy with vacuolation.	49

inflammatory markers and cytokines are frequently observed in the context of aluminium exposure, further harming neurons (26).

6.4. Neurochemical changes

Chronic exposure to $AlCl_3$ leads to alterations in neurotransmitter levels, particularly acetylcholine, which is crucial for cognitive processes. These changes can damage synaptic plasticity and impair long-term potentiation, both of which are vital for learning and memory (29).

6.5. Histopathological changes

Histological studies have shown that $AlCl_3$ exposure induces severe neuronal damage, including necrosis, vacuolation, and karyolysis, particularly in the hippocampal region. These changes are indicative of profound cellular damage and contribute to the neurodegenerative effects of aluminium toxicity (30).

7. Risk Assessment and neurotoxic effects of aluminium chloride exposure

Assessing the risks associated with aluminium chloride ($AlCl_3$) exposure is crucial for understanding its long-term impact on brain health. Aluminium chloride is known to induce significant neurotoxic alterations in the brain, particularly affecting brain structures like the cerebral cortex and hippocampus. This section examines the specific neurotoxic effects of $AlCl_3$, including the mechanisms driving these changes, such as oxidative stress, blood-brain barrier dysfunction, and neuronal damage. The evaluation is based on histological findings and neurotoxicological studies, providing a comprehensive risk assessment of the potential impacts of $AlCl_3$ on brain structure and function.

7.1. Histological changes

Aluminium chloride ($AlCl_3$) exposure induces significant disruptions in the structural integrity of the brain, particularly in the cerebral cortex. One of the most prominent histological changes observed is the dissolution of the laminated structure of the cortex.

This results in the formation of vacuoles and cellular damage, which serve as clear markers of the neurotoxic effects of aluminium on brain tissue (31). These structural disruptions are indicative of the severity of aluminium's impact on the brain.

In addition to these disruptions, neuronal damage is a significant consequence of chronic $AlCl_3$ exposure. Prolonged exposure leads to extensive neuronal degeneration, especially in the hippocampus, a region vital for learning and memory processes. This degeneration results in cognitive impairments, as observed in animal models subjected to high levels of aluminium (32). The neuronal damage in the hippocampus plays a crucial role in the cognitive deficits linked to aluminium toxicity.

7.2. Neurotoxic effects

The neurotoxic effects of $AlCl_3$ are primarily mediated through several key mechanisms, one of which is blood-brain barrier dysfunction. $AlCl_3$ has been shown to disrupt the blood-brain barrier (BBB), allowing aluminium to accumulate within the brain. This breach in the barrier enhances the risk of neurodegenerative diseases, including Alzheimer's disease, as aluminium interferes with normal brain functions (25-27). The accumulation of aluminium within the brain tissues further exacerbates its neurotoxic effects, contributing to neuronal damage and cognitive decline.

Another significant effect of $AlCl_3$ exposure is cell death within neuronal tissues. This is typically manifested through necrosis and cytoplasmic vacuolation, both of which highlight the severe neurotoxic potential of aluminium (32). These cellular changes are indicative of the profound damage inflicted on the brain by prolonged aluminium exposure.

Moreover, neurodegeneration acceleration is a notable consequence of long-term $AlCl_3$ exposure. Chronic exposure has been linked to an accelerated process of neuronal aging and senescence, leading to an earlier onset of neurodegenerative diseases such as Alzheimer's and Parkinson's disease (32-34). The faster progression of these diseases is attributed to the cumulative damage caused by prolonged aluminium toxicity.

7.3. Age-Dependent vulnerability

Age plays a critical role in the susceptibility to $AlCl_3$-induced neurotoxicity. Younger animals, particularly those aged 1-2 months, are more vulnerable to the neurotoxic effects of $AlCl_3$ compared to older animals. This age-dependent vulnerability emphasizes the importance of considering age-related factors when evaluating the severity of aluminium-induced neurotoxicity (31). Younger brains may have a heightened sensitivity to the toxic effects of aluminium, potentially leading to more pronounced damage and earlier onset of neurodegenerative conditions.

The neurotoxic effects of aluminium chloride ($AlCl_3$) were observed across various animal models with different doses and durations of exposure. Key findings include:

- 17 mg/kg for 21-28 days: Induced blood-brain barrier disruption, immune cell infiltration, neuronal damage, and liver enzyme elevation, with edema observed in both perineural and perivascular regions.
- 50 mg/kg for 28 days: Resulted in significant changes in the hippocampus, including increased eosinophilic and β-amyloid plaque deposits.
- 100 mg/kg for 21-60 days: Led to significant histopathological changes, including neurodegeneration, neuronal necrosis, and apoptosis, with elevated caspase-3 levels and increased amyloid precursor protein (APP) expression.
- 150 mg/kg for 90 days: Caused significant biochemical and neurochemical alterations linked to cognitive decline, with observable damage to brain chemistry and cellular processes.
- 175 mg/kg for 60 days: Showed extensive neuronal degeneration, including shrunken and blackened neurons in the cerebral cortex, accompanied by neuronophagia

and gliosis.

- 200 mg/kg for 14-60 days: Caused severe neuronal degeneration, increased apoptotic markers, and marked structural damage in brain regions such as the hippocampus and cerebral cortex.
- 300 mg/kg for 60 days: Led to significant damage in hippocampal regions, including pyknotic neurons, decreased mature pyramidal cells, and structural disorientation, contributing to cognitive impairments.
- Higher doses (up to 200 mg/kg for 8 weeks): Resulted in significant neuronal loss, amyloid deposition, and apoptosis, particularly in the hippocampal regions CA1 and CA3.

Therefore, longer exposure durations and higher doses of $AlCl_3$ consistently led to more severe neurodegenerative effects, including neuronal apoptosis, amyloid plaque formation, and cognitive impairments, suggesting that prolonged and high-dose exposure to $AlCl_3$ can have a profound impact on brain structure and function.

8. Conclusion

In conclusion, Aluminium chloride ($AlCl_3$) is a potent neurotoxicant that significantly impacts brain structure and function, particularly through mechanisms involving oxidative stress, neuronal damage, and cellular dysfunction. Chronic exposure to $AlCl_3$ leads to the generation of reactive oxygen species (ROS), lipid peroxidation, and a reduction in antioxidant defenses, all of which contribute to the degradation of brain cells and cognitive impairments. The histopathological alterations observed, such as necrosis, cytoplasmic vacuolations, and karyopyknosis, further support the neurotoxic effects of aluminium exposure. Additionally, $AlCl_3$ disrupts key cellular organelles, including mitochondria, the nucleus, and the endoplasmic reticulum, exacerbating oxidative stress and promoting neurodegenerative processes. Genetic changes, such as alterations in the expression of cyclin D1, p21, and Nrf2, underscore the complex interactions between aluminium and cellular mechanisms regulating the cell cycle and oxidative stress responses. Moreover, the potential disruption of the blood-brain barrier by $AlCl_3$ raises significant concerns about the long-term consequences of aluminium exposure on brain health. These findings highlight the need for continued research into the effects of aluminium chloride on the nervous system and its potential contribution to neurodegenerative diseases, emphasizing the importance of addressing environmental and occupational exposures to this neurotoxicant.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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