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Original Research Article

Cognito-Motor and Neuro-Behavioural Modulatory Action of Lutein on BDNF-α Activities in Aluminium Chloride-Induced Memory Impaired Mice

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Abstract: Lutein enhances Cognito-motor and neuro-behavioural processes by modulating BDNF-α activity in a mouse model with memory impairment caused by aluminum chloride ($AlCl_3$). Aluminium chloride neurotoxicity frequently leads to cognitive abnormalities similar to Alzheimer's. Neurotrophin variation of BDNF-α, plays key roles in synaptic plasticity, and cognitive functions. This study aims to evaluate the Cognito-motor and neuro-behavioural modulatory action of lutein on BDNF-α activities in $AlCl_3$-induced memory-impaired mice. 30 adult Mice (30kg) were randomly divided into six groups and treated for three weeks: Group 1 (Negative Control), Group 2 (100mg/kg-$AlCl_3$), Group 3 (100mg/kg-$AlCl_3$ + 20mg/kg-Lutein), Group 4 (100mg/kg-$AlCl_3$ + 40mg/kg-Lutein), Group 5 (100mg/kg-$AlCl_3$ + 60mg/kg-Lutein), Group 6 (100mg/kg-$AlCl_3$ + 5mg/kg-Donepezil). Neurobehavioral activities (Barnes, Y-maze, handgrip and Rotarod) were recorded and analyzed using ANOVA. Ethical approval for this research was obtained from the University of Port Harcourt ethics committee. In Barnes maze test, Group 2 and 3 showed significantly increased escape times ($p<0.0001$, $p<0.05$) compared to control for week 2 and 3. Hand grip test showed decreased in grip strength in Group 2 ($p<0.0001$), and reduced navigation time in Group 3 ($p<0.05$). Rotarod tests indicated reduced stability time and Y-maze test showed increase in inflexion ratio in Groups 2 and 3. In BDNF-α level, Group 2 and 3 had a significant reduction ($p < 0.0001$ and $p < 0.001$) respectively. Aluminum chloride intake reduced BDNF-α level, negatively impacting Cognito-motor performance. Lutein administration increased cognitive and behavioral performance through BDNF-α modulation. The group receiving both treatments showed a notable increase in BDNF-α level and cognitive performance. Hence, lutein significantly mitigates Aluminium Chloride-induced neurotoxicity and cogni-motor dysfunction in mice through antioxidant, anti-inflammatory, and neurotrophic mechanisms, placing it as a promising natural alternative or adjunct therapy for neurodegenerative disorders like Alzheimer's and Parkinson's disease.
Keywords: Lutein; BDNF-α, Aluminium Chloride, Neuroprotection, Alzheimer's Disease.

INTRODUCTION

An adult human brain maintains over 100 billion neurons to operate as the control center which manages cognitive and physiological functions including movement and senses and emotions and language and memory (Stiles & Jernigan, 2014; Maldonado & Alsayouri, 2023). Its three main parts - the cerebrum, cerebellum, and brainstem, each play critical roles in overall functioning. The cerebral cortex controls awareness and communication and memory functions alongside vision and language and voluntary movements yet the cerebellum maintains control over motor movements and balance (Moini *et al*., 2021; Roostaei *et al*., 2014). The brain's intricate neuronal networks underpin all aspects of behavior, cognition, and motor activity (Maldonado & Alsayouri, 2023).

The development of long-term memory together with developmental capabilities depends on the functional relationship between hippocampus and prefrontal cortex (Squire, 2019; Preston & Eichenbaum, 2015). Quality of life suffers substantially from memory and cognitive decline that frequently arises due to trauma alongside neurodegenerative diseases and neurotoxic exposure (Nataraj *et al*., 2016; Crawford & Loprinzi, 2019). Studies link aluminum chloride ($AlCl_3$) to neurodegenerative changes and memory deficits and

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cognitive impairments while also causing oxidative stress and disrupting neurochemical pathways (Zatta *et al*., 2022; L. Zhang *et al*., 2014).

The protein Brain-Derived Neurotrophic Factor (BDNF) maintains critical functions for both viable neurons and learning processes thus protecting mental abilities along with neural flexibility (Ismail *et al*., 2020). BDNF expression faces threats from environmental toxins like $AlCl_3$ because these toxins create oxidative stress and inflammation while causing cognitive decline that worsens Alzheimer's disease pathology (Miyanishi & Nitta, 2021; Shunan *et al*., 2021).

The brain tissue contains high amounts of lutein which functions as a protective molecule for cognitive function while also defending against oxidative damage (Renzi *et al*., 2014; Erdman *et al*., 2015). Research continues to investigate the unknown mechanisms by which lutein defends against $AlCl_3$-induced cognitive impairments despite its proven impact on neural health enhancement (Geiss *et al*., 2019).

It has been widely established that memory impairment and neurodegenerative diseases are linked to chemicals in the environment and free radicals. Aluminum chloride is neurotoxic and disrupts cognition and behaviour by damaging neurons. An antioxidant lutein may protect cognitive functions by being involved in the regulation of Brain-Derived Neurotrophic Factor-alpha (BDNF-α) which is vital in the brain. This study examines lutein effects on BDNF-α in aluminum chloride-induced memory impaired mice to understand the treatment for cognitive dysfunction.

Null Hypothesis (H0):

Lutein administration has no effect on cognitive, motor, or neuro-behavioral outcomes, and does not alter BDNF-α activities in aluminum chloride-induced memory-impaired mice.

Alternative Hypothesis (H1):

Lutein administration significantly improves cognitive, motor, and neuro-behavioral outcomes by enhancing BDNF-α activities in aluminum chloride-induced memory-impaired mice.

The primary aim of this study is to evaluate the Cognito-Motor and Neuro-Behavioural Modulatory Action of Lutein on BDNF-α Activities in Aluminium Chloride-Induced Memory Impaired Mice.

The specific objectives are as follows:

1. To investigate the effects of lutein on cognitive impairments induced by aluminum chloride in mice, using the Barnes Maze and Y-Maze neurobehavioral tests.
2. To assess the role of lutein in alleviating motor impairments caused by aluminum chloride in mice, using the Handgrip and Rotarod neurobehavioral tests.
3. To explore the potential of lutein to modulate BDNF-α expression in aluminum chloride-induced memory-impaired mice.
4. To examine the impact of aluminum chloride exposure on BDNF-α activity and cognitive behavior in mice.
5. To evaluate neurobehavioral outcomes, including motor function and spatial memory, following lutein supplementation in aluminum chloride-induced memory-impaired mice.
6. To determine the effects of oral lutein administration on memory impairment caused by aluminum chloride exposure in mice.
7. To investigate the neuroprotective potential of lutein on brain tissue in mice treated with aluminum chloride.

MATERIALS AND METHODS

Chemicals and Reagents

The chemicals and reagents used for this study were purchased from GGI Intl' Nigeria Ltd. located at GGI Place, Plot 8 GGI Crescent, (Opp. Mikab Filling Station), Port Harcourt, Rivers State, Nigeria. The chemicals and reagents are as follows:

a. **Lutein:** High-purity lutein was obtained in three different concentrations to create low (20mg/kg), medium (40mg/kg), and high (60mg/kg) lutein dose groups. It was administered orally using a canula.
b. **Aluminium chloride ($AlCl_3$):** Aluminium chloride ($AlCl_3$) was used to induce neurotoxicity and memory impairment in the experimental mouse model. A dose of 100 mg/kg body weight was selected based on previous studies that demonstrated this dose reliably induces cognitive impairment and oxidative stress in rodents (Firdaus *et al*., 2022). 0.5ml was administered to the mice orally using a canula.
c. Assay kits for BDNF, acetylcholinesterase (AChE), and malondialdehyde (MDA) levels
d. **Donepezil:** Donepezil, an acetylcholinesterase inhibitor, served as the standard drug for comparison. It was also administered orally.
e. **Anaesthesia:** Diethyl ether was use to anesthetize the mice during the surgical procedures.
f. **Apparatus for behavioral tests:** Including Barnes Maze test, Y maze test, Hand grip and Rotarod.
g. **Surgical instruments:** For tissue harvesting and sampling.
h. **Standard laboratory supplies:** Including syringes, needles, bottles and other consumables.

Experimental Design

A total of 30 Mice were randomly selected and divided into six groups of 5 Mice per group. The

administration took 21 consecutive days within the hours of 8:00 to 10:00am daily. Aluminum Chloride was administered 30-60mins before the administration of lutein. Then 30 minutes later Neurobehavioral tests was conducted. They were treated for three weeks thus: Group 1 (control), Group 2 (0.5ml of Aluminum Chloride only of dose 100mg/kg), Group 3 (0.5ml of $AlCl_3$ + 0.5ml of lutein low dose (20mg)), Group 4 (0.5ml of $AlCl_3$ + 0.5ml of lutein medium dose (40mg), Group 5 (0.5ml of $AlCl_3$ + 0.5ml of lutein high dose (60mg)), and Group 6 (0.5ml of $AlCl_3$ + 0.3ml of Donepezil). The experimental design is as summarized in table 1 below.

Table 1: The experimental design showing the group, treatment, test, procedure and duration.

Groups	Treatment	Neuro-Behavioural test	Procedure and Duration
Group 1 (5 mice)	Control	Barnes maze test, Y maze test, handgrip test and Rotarod.	The rats were exposed to the cognitive test without any drug treatment for a period of 3 weeks
Group 2 (5 mice)	0.5ml of Aluminium Chloride only of dose 100mg/kg	Barnes maze test, Y maze test, handgrip test and Rotarod.	The rats were exposed to the cognitive test with 0.5 ml of $AlCl_3$ for a period of 3 weeks
Group 3 (5 mice)	0.5ml of AlCl3 + 0.5ml of lutein low dose (20mg)	Barnes maze test, Y maze test, handgrip test and Rotarod.	The mice were exposed to the cognitive test with 0.5ml of $AlCl_3$ + 0.5ml of lutein low dose (20mg) for a period of 3 weeks
Group 4 (5 mice)	0.5ml of AlCl3 + 0.5ml of lutein medium dose (40mg)	Barnes maze test, Y maze test, handgrip test and Rotarod.	The rats were exposed to the cognitive test with 0.5ml of $AlCl_3$ + 0.5ml of lutein medium dose (40mg) for a period of 3 weeks
Group 5 (5 mice)	0.5ml of AlCl3 + 0.5ml of lutein high dose (60mg) 5 mice	Barnes maze test, Y maze test, handgrip test and Rotarod.	The mice were exposed through the cognitive test with 0.5ml of $AlCl_3$ + 0.5ml of lutein high dose (60mg) for a period of 3 weeks
Group 6 (5 mice)	0.5ml of AlCl3 + 0.3ml of Donepezil	Barnes maze test, Y maze test, handgrip test and Rotarod.	The mice were exposed through the cognitive test with 0.5ml of $AlCl_3$ + 0.3ml of Donepezil for a period of 3 weeks

Statistical Analysis

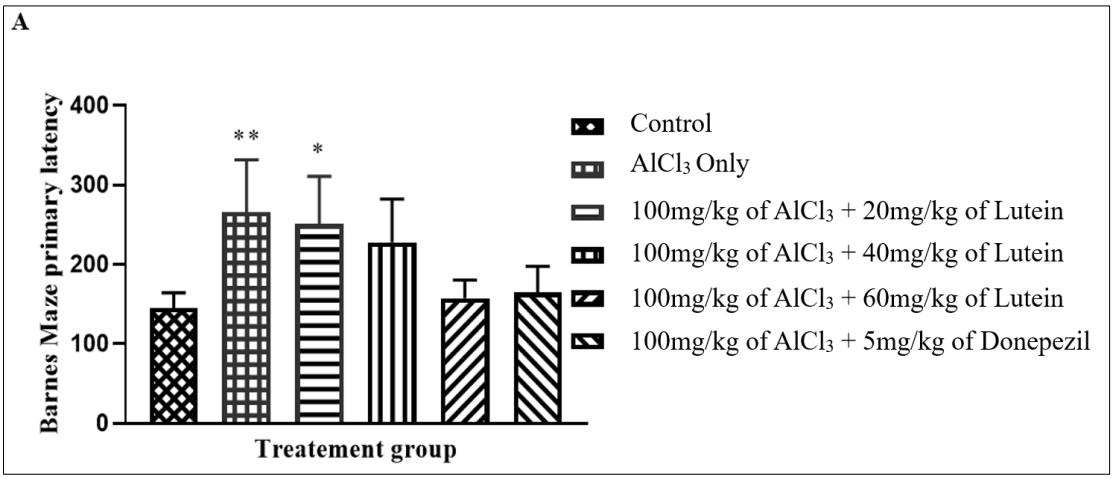
Statistical data were analyzed using GraphPad Prism 8 software (Graph-pad Software Inc., San Diego, USA). Multiple-group parametric data were analysed by one-way analysis of variance (ANOVA), expressed as mean standard deviation (SD); followed by a Tukey's post hoc test for multiple group comparisons. Data was considered statistically significant when $p \leq 0.05$.

RESULTS AND DISCUSSIONS

Results

The experimental groups in this study were categorized as follows:

Group 1: Negative Control
Group 2: Aluminium Chloride
Group 3: Aluminium Chloride + lutein (20mg/kg)
Group 4: Aluminium Chloride + lutein (40mg/kg)
Group 5: Aluminium Chloride + lutein (60mg/kg)
Group 6: Aluminium Chloride + Donepezil (5mg/kg - Standard Drug)



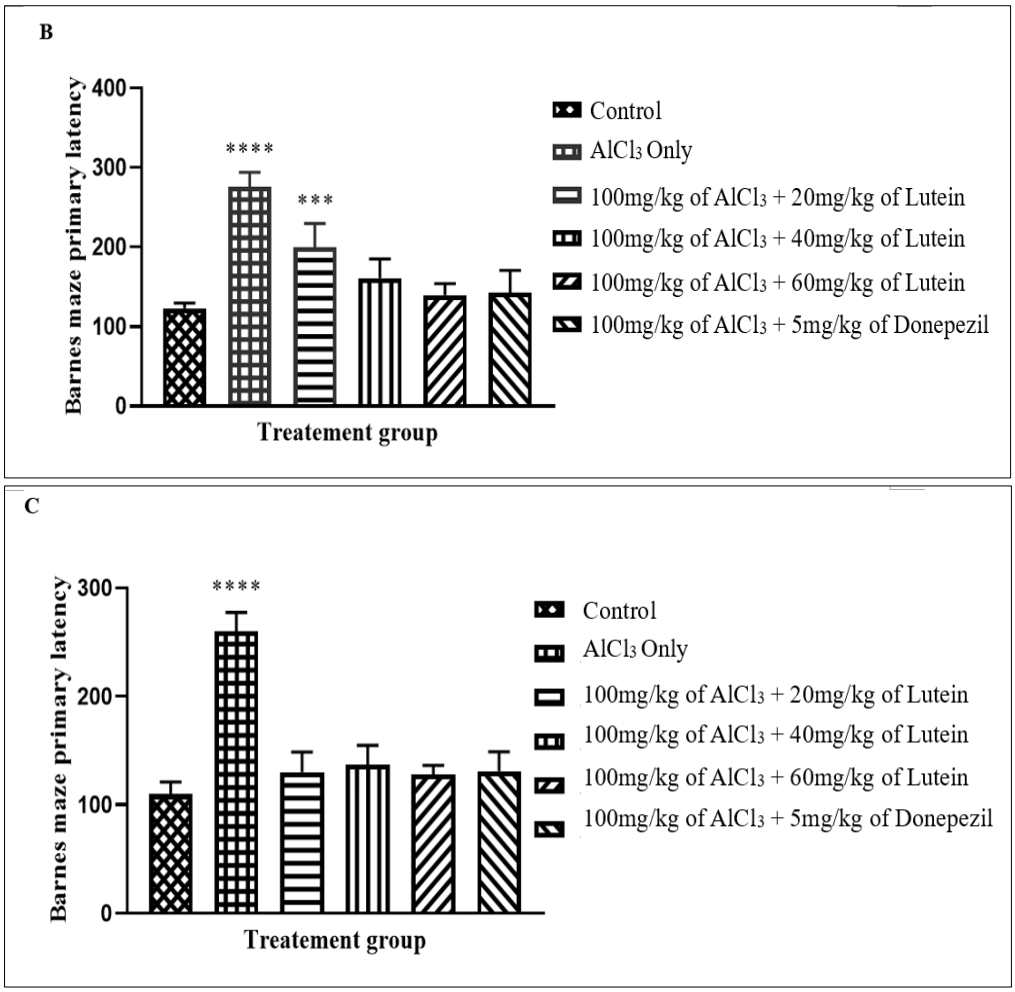


Figure 1: Effect of Lutein on Barnes Maze Primary Latency in Aluminium Chloride- Induced Memory-Impaired Mice. A = Week 1, B = Week 2, and C = Week 3); Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at P < 0.05, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001.

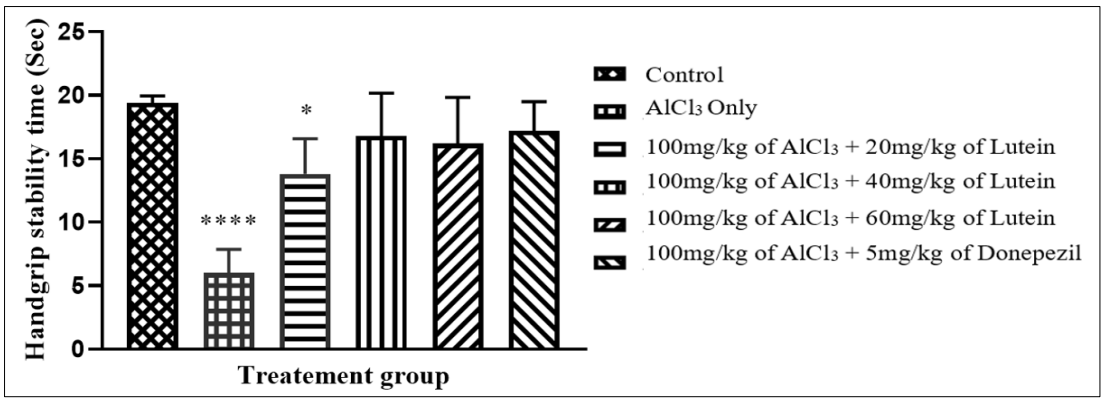


Figure 2: Effect of Lutein on Handgrip stability time in Aluminium Chloride-Induced Memory-Impaired Mice. Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at P < 0.05, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001.

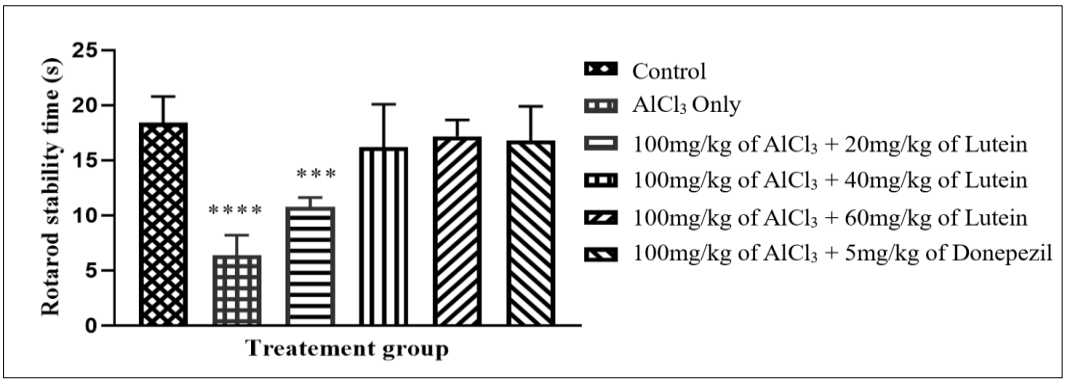


Figure 3: Effect of Lutein on Rotarod stability time in Aluminium Chloride-Induced Memory-Impaired Mice. Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at P < 0.05, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001.

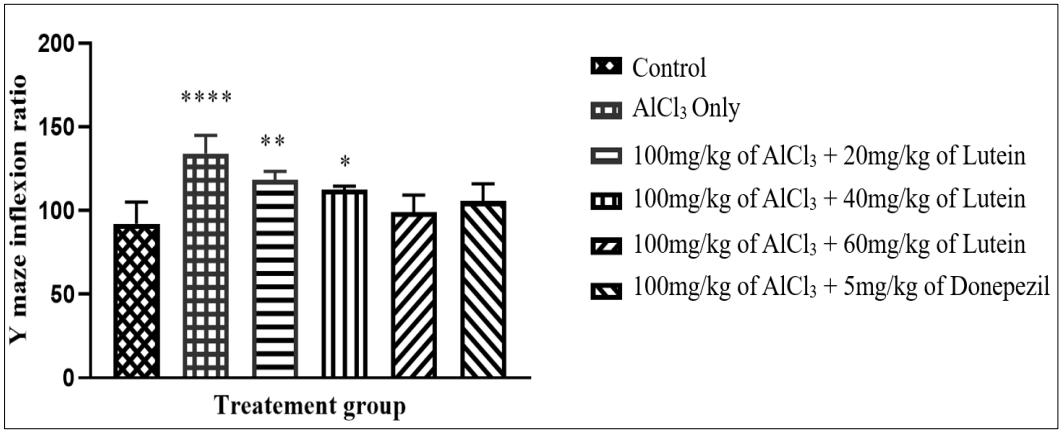


Figure 4: Effect of Lutein on Y-maze inflexion ratio in Aluminium Chloride-Induced Memory-Impaired Mice. Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at P < 0.05, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001.

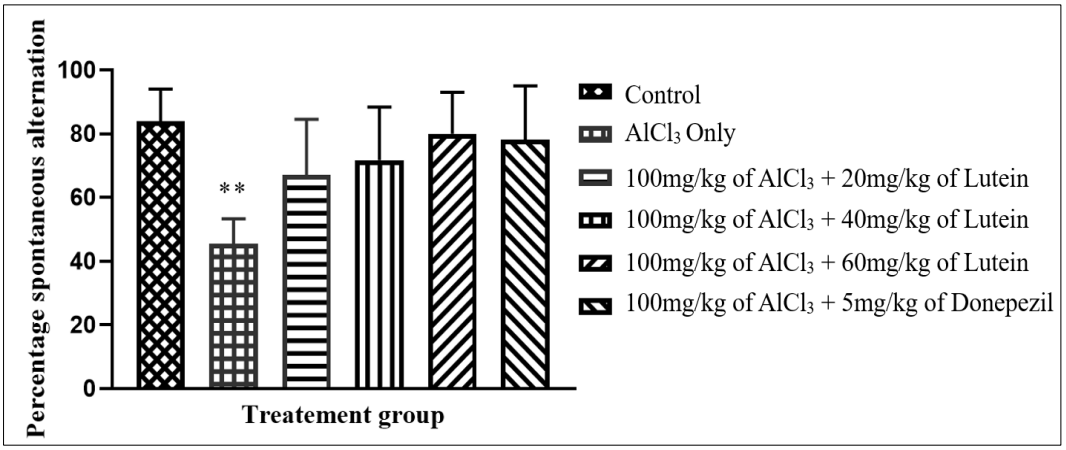


Figure 5: Effect of Lutein on Y-maze percentage of spontaneous alternation in Aluminium Chloride-Induced Memory-Impaired Mice. Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at $P < 0.05$, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001.

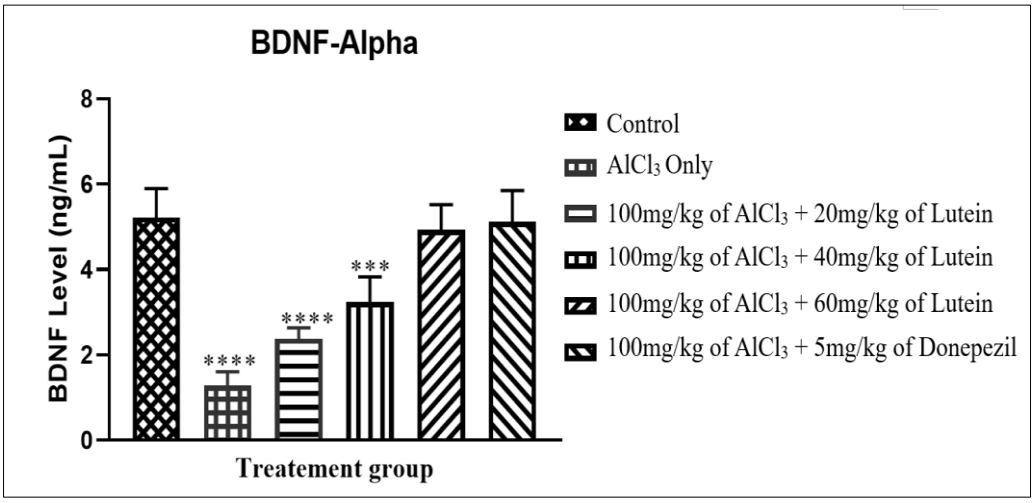


Figure 6: Effect of Lutein on BDNF-α Levels in Aluminium Chloride-Induced Memory- Impaired Mice. Results are presented as mean ± SEM. N=5.

The columns represent the mean values and error bars indicate the Standard deviation (SD) of our independent experiments. * Indicates statistical significance of Aluminum Chloride and treatments versus the Negative controls * significant at $P < 0.05$, ** significant at 0.01, *** significant at 0.001 and **** significant at 0.0001

DISCUSSION

The Barnes Maze Test

As presented in Figure 1, the result shows the effect of lutein on $AlCl_3$ induced memory deficits in mice over three weeks. This was judged by the fact that the mice treated with $AlCl_3$ alone had the longest primary latency, suggesting that the animals had poor spatial learning and memory as a result of neurotoxicity to the hippocampus. This impairment became progressively worse, indicating that chronic toxic effects were being accumulated.

Treatment with lutein showed dose-dependent neuroprotection:

- Low-dose Lutein (20mg/kg): Some degree of memory enhancement was observed; however, memory was still suboptimal in comparison to the control group.
- Medium-dose Lutein (40mg/kg): Moderate improvement, approaching the control level at Week 3.
- High-dose Lutein (60mg/kg): The scores as obtained in the control group during the entire period of the study, showing that the memory was fully restored during each of the weeks.

The effectiveness of high-dose lutein was as effective as the standard neuroprotective therapy (Donepezil, 5mg/kg), making lutein a potential alternative treatment.

The results are consistent with previous studies (Nazari *et al.,* 2022), where lutein effects were established antiradical potential and protection against oxidative damage, inhibiting neurotoxicity and promoting cognitive function in neurological disorders. Lutein is revealed to possess some therapeutic value in combating the problem of cognitive loss in the researchers study.

Handgrip Stability Test

The result presented in Figure 2 indicates that Lutein significantly increased the handgrip stability time in $AlCl_3$ - induced memory impaired mice suggesting its possible neuroprotective action. The data are presented as mean ± SEM and statistical significance was determined by comparison to a control group.

The control group had the longest stability time (~20 sec) for handgrip, which set the standard for normal motor coordination. $AlCl_3$ treated mice at a dose of 100 mg/kg significantly reduced the grip stability to around 6 seconds which is quite different from the control group ($P < 0.0001$) and thus showing neurotoxicity of $AlCl_3$ mediated through oxidative stress, neuro inflammation and impaired neuromuscular function.

Lutein at 20 mg/kg (low dose) somewhat ameliorated the effect of $AlCl_3$ on handgrip time to $P < 0.05$ but not to the normal level. At 40 mg/kg (medium dose), Lutein improved grip stability to near control (~20) suggesting strong neuroprotection which could be

attributed to its modulation of BDNF-α signaling and antioxidant activity. High-dose Lutein showed similar recovery as the control, implying that there is an upper limit as to how much improvement can be gained.

These outcomes confirm that Lutein only at the higher dosage significantly ameliorates $AlCl_3$-evoked motor dysfunction and strengthens the rationale of using Lutein as a therapeutic option for neurodegenerative disorders. These findings are consistent with prior research by Nataraj *et al*., (2016) who showed that Lutein has a neuroprotective effect which can reduce mitochondrial dysfunction, oxidative stress and motor deficits.

Rotarod Stability Time Test

This graph presents the rotarod stability time for different treatment groups in Aluminium chloride ($AlCl_3$)-induced memory-impaired mice. The Negative Control group exhibits the highest rotarod stability time (~20 seconds), indicating normal motor coordination and balance. Mice treated with 100mg/kg of Aluminium Chloride only, demonstrates a significantly reduced stability time (~7-8 seconds; **** $P < 0.0001$), reflecting impaired motor coordination caused by $AlCl_3$-induced neurotoxicity. Low Dose (20 mg/kg): Moderate improvement in stability time (~12 seconds; ***$P < 0.001$), indicating partial amelioration of motor deficits. Medium Dose (40 mg/kg): Further improvement (~18 seconds), approaching the control level, suggesting enhanced protective effects. High Dose (60 mg/kg): Nearly restores stability time (~20 seconds) to the control group level, suggesting optimal neuroprotective efficacy.

Mice treated with 100mg/kg of Aluminum Chloride and 5mg/kg of Donepezil (Standard Treatment) has a comparable improvement to the high-dose lutein group (~20 seconds), indicating a similar level of therapeutic efficacy.

Y-Maze Inflexion Ratio

Figure 4 shows a graphical representation of Y-maze Y-maze inflexion ratio across different treatment groups in Aluminium chloride ($AlCl_3$)-induced memory-impaired mice. The Y-maze inflexion ratio is a behavioral metric used to assess spatial working memory and exploratory behavior.

- Control Group: had the lowest inflexion ratio (~90), which represents the baseline exploratory activity and memory performance of healthy, untreated mice.
- $AlCl_3$-Only Group: showed a significantly increased inflexion ratio (~150; ****$P < 0.0001$), indicating hyperactivity or disrupted exploratory patterns due to neurotoxicity. This suggests $AlCl_3$ impairs spatial memory or causes compensatory hyperactivity.
- Low Dose lutein (20 mg/kg): Shows partial reduction in inflexion ratio (~120; $P < 0.01$), indicating some recovery in memory performance or behavioral normalization.
- Medium Dose lutein (40 mg/kg): Further improvement, with a ratio closer to normal (~110; $P < 0.05$), indicating enhanced efficacy.
- High Dose lutein (60 mg/kg): Reaches levels similar to the control group (~100), suggesting near- complete reversal of $AlCl_3$-induced deficits.
- Mice treated with Aluminum Chloride (100mg/kg) and Donepezil (5mg/kg) (Standard Treatment) is comparable to the high-dose lutein group (~100), indicating effective mitigation of memory impairment and behavioral normalization.

By inflexion ratios, the result reveals that $AlCl_3$ neurotoxicity affects working memory and exploratory behavior in rats. Lutein dose-dependently ameliorates these effects, with high doses nearly normalizing memory and exploratory activity. The high dose Lutein group (60 mg/kg) has the same efficacy score as Donepezil indicating the neuroprotective effects of Lutein. This effect is perhaps due to Lutein's antioxidant properties, its anti-inflammatory action, and its promotion of brain-derived neurotrophic factor (BDNF).

Maze Spontaneous Alternation

The Y-Maze Spontaneous Alternation test is a widely used behavioral test in neuroscience to assess spatial working memory and cognitive flexibility in rodents (mice or rats). The maze is shaped like a "Y," with three arms (usually labeled A, B, and C). An elevated spontaneous alternation percentage indicates enhanced working memory and cognitive flexibility. This suggests that the Mice can effectively remember which arms it has already visited, also the neural pathways involved in memory and exploration such as hippocampus and prefrontal cortex are functioning well. While a reduced spontaneous alternation percentage in the Y-Maze Spontaneous Alternation test indicates impairments in spatial working memory and cognitive flexibility.

The graph in Figure 5 presents the effect of lutein treatment on the percentage of spontaneous alternation in the Y-maze test for mice with $AlCl_3$-induced memory impairment. This parameter is a widely used indicator of spatial working memory, which is dependent on hippocampal function. The negative control group exhibits the highest percentage of spontaneous alternation (~80%), suggesting normal spatial working memory and hippocampal function. This serves as the baseline for comparison with other groups.

- $AlCl_3$ Only: Shows a significant reduction in spontaneous alternation (~60%), with $p < 0.01$. This indicates severe impairment in spatial working memory, consistent with AlCl3-induced neurotoxicity, likely due to oxidative stress and hippocampal damage.
- Lutein Low Dose (20 mg/kg): The percentage

of alternation improves slightly compared to the $ALCl_3$-only group but remains below control levels. This indicates partial restoration of memory performance, suggesting mild neuroprotection at this dose.

- Medium Dose (40 mg/kg): A marked improvement is observed, with percentages approaching the control group. This suggests that the medium dose effectively counters AlCl3-induced neurotoxicity and restores spatial working memory.
- High Dose (60 mg/kg): The percentage of spontaneous alternation is comparable to the control group, indicating full recovery of spatial working memory. This supports the hypothesis that lutein's neuroprotective effects are dose-dependent.
- Mice treated with 100mg/kg of Aluminium chloride and 5mg/kg of Donepezil shows similar performance to the high- dose lutein group, further confirming the efficacy of lutein as a potential neuroprotective agent comparable to the standard drug

Brain Derived Neurotrophic Factor-Alpha (BDNF-α)

Figure 6 examines the impact of Lutein treatment on brain-derived neurotrophic factor-alpha (BDNF-α) levels in mice subjected to neurotoxicity induced by Aluminium Chloride ($AlCl_3$). The findings highlight the neurorestorative potential of Lutein, as shown by its dose-dependent modulation of BDNF-α levels.

- Negative Control Group: exhibits the highest BDNF-α levels (~6 ng/mL), representing the baseline expression of this neurotrophic factor under normal physiological conditions. This group serves as the standard, showcasing optimal neuroprotective signaling in the absence of AlCl3 exposure or treatment intervention.
- $AlCl_3$-Only Group: BDNF-α levels are significantly reduced (~1.5 ng/mL) in the AlCl3-only group, with a $P < 0.0001$ (indicated by ****). This severe decline reflects the neurotoxic effects of $AlCl_3$, which suppresses BDNF expression, likely due to oxidative stress, neuroinflammation, and mitochondrial dysfunction. These effects impair neuronal survival and synaptic integrity, critical for memory and cognitive processing.
- In Mice treated with Low Dose of lutein (20mg/kg): A modest increase in BDNF-α levels (~3.5 ng/mL) compared to the $AlCl_3$-only group is observed, with statistical significance at $**P < 0.001$ (indicated by *). Although levels remain below the control, this partial recovery suggests that low doses of lutein mitigate the neuro toxic effects of $AlCl_3$, likely through its antioxidative and anti- inflammatory properties.
- Medium Dose of lutein (40mg/kg): BDNF-α levels (~6 ng/mL) are fully restored to control levels, indicating near-complete recovery of neurotrophic signaling. The absence of statistical markers relative to the control implies no significant difference between the medium-dose group and the untreated healthy group. This suggests that medium doses of Lutein effectively counteract $AlCl_3$-induced suppression of BDNF.
- High Dose of lutein (60mg/kg): Similar to the medium dose, high-dose treatment results in BDNF-α levels comparable to the control group (~6 ng/mL). This supports the idea that a therapeutic threshold of Lutein dosage is required to normalize neurotrophic signaling.
- Aluminium chloride (100mg/kg) and 5mg/kg of Donepezil: Shows a similar level of BDNF-α recovery (~6 ng/mL). This suggests that Lutein's effects are on par with standard neuroprotective intervention.

CONCLUSION

The findings of this study have provided significant insights into the neuroprotective effects of lutein in mitigating $AlCl_3$-induced neurotoxicity and cognitive impairment in a mice model. The results collectively underscore lutein's therapeutic potential as a natural agent for preventing and managing cognitive decline, motor dysfunction, and oxidative stress-induced neuronal damage, which are hallmarks of neurodegenerative disorders.

The behavioral analyses demonstrated that $AlCl_3$ exposure led to significant impairments in memory, motor function, and neuromuscular strength, as evidenced by poor performance in the Y- maze, Barnes maze, rotarod, and hand grip tests. These outcomes reflect $AlCl_3$'s detrimental effects on spatial working memory, motor coordination, and neuromuscular endurance. Importantly, lutein supplementation at medium (40 mg/kg) and high (60 mg/kg) doses significantly reversed these deficits, bringing the performance of treated mice closer to that of the control group. High-dose lutein, in particular, showed comparable efficacy to Donepezil, the standard treatment, suggesting that lutein could serve as a promising alternative or adjunctive therapy for neurodegenerative conditions.

The study further revealed that lutein's neuroprotective effects are mediated through its ability to modulate brain-derived neurotrophic factor-alpha (BDNF-α) activity. BDNF-α is a critical neurotrophin involved in synaptic plasticity, neuronal survival, and memory formation. $AlCl_3$- induced neurotoxicity led to a marked reduction in BDNF-α levels, consistent with neuronal dysfunction and memory impairment. However, lutein treatment restored BDNF-α activity in a dose-dependent manner, highlighting its potential to enhance neurogenesis and synaptic resilience.

Histological analyses corroborated these findings by demonstrating reduced neuronal damage and preservation of hippocampal architecture in lutein-treated groups. These outcomes further confirm lutein's role in countering $AlCl_3$-induced oxidative stress, neuroinflammation, and cellular apoptosis, which are key drivers of neurodegeneration. The comparison between lutein and Donepezil provided valuable insights into their relative efficacies. While Donepezil, a cholinesterase inhibitor, primarily targets neurotransmitter systems to improve cognitive function, lutein exerts its effects through a multifaceted mechanism involving antioxidant activity, modulation of neurotrophic factors, and anti-inflammatory properties. The comparable performance of high-dose lutein to Donepezil underscores its potential as a natural, non-toxic alternative, particularly for individuals who may experience side effects or contraindications with synthetic drugs.

The outcomes of this study have significant implications for the management of neurodegenerative disorders, such as Alzheimer's disease (AD) and Parkinson's disease (PD), which are characterized by progressive cognitive and motor impairments. The ability of lutein to improve spatial memory, motor coordination, and neuronal survival suggests that it could play a pivotal role in slowing disease progression and enhancing the quality of life for affected individuals. As a carotenoid abundant in dietary sources like green leafy vegetables and eggs, lutein represents an accessible and cost-effective intervention for promoting brain health. Its natural origin, combined with its broad spectrum of protective effects, makes it a particularly attractive candidate for preventive strategies in populations at risk of developing neurodegenerative diseases.

In conclusion, this study highlights lutein as a promising neuroprotective agent capable of mitigating the deleterious effects of $AlCl_3$-induced neurotoxicity. Its dose-dependent efficacy in improving cognitive and motor functions, coupled with its molecular and histological benefits, positions it as a viable alternative or complement to conventional treatments for neurodegenerative disorders.

However, while the findings are promising, further research is warranted to address the limitations identified in this study and to explore lutein's therapeutic potential in greater depth. Future studies should focus on:

1. Long-term studies to assess the sustainability of lutein's neuroprotective effects.
2. Exploration of synergistic effects between lutein and other neuroprotective agents.
3. Clinical trials to validate the translational potential of lutein in human populations.
4. Mechanistic studies to unravel additional pathways influenced by lutein.

The findings presented herein contribute to the growing body of evidence supporting the role of natural antioxidants in the prevention and management of neurodegenerative disorders, offering new hope for addressing the global burden of cognitive decline.

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