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Virgin Coconut Oil Ameliorates Cognitive Impairment in Alzheimer's-Like Rats Induced with Aluminium Chloride ($AlCl_3$) + D-Galactose (D-Gal)

Onesimus Mahdi[1], Simeon Benjamin[2], Khadijat Abubakar Bobbo[3], Abel Nosoreme Agbon[4], Lawan Ibrahim Aliyu[5], Kuchahyells Mathias[6], Anathoth Alhassan[7], Deborah Dilla[8], Raphael Reseph[9]
[1,2,5,6,7,8,9]Gombe State University, Gombe, Nigeria; [3]Universiti Putra Malaysia, Selangor, Malaysia; [4]Ahmadu Bello University Zaria, Nigeria
omahdi2010@gmail.com; khadijanti@gmail.com

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Abstract

Neurodegenerative diseases are a group of disorders marked by the progressive deterioration of neurons in the brain and spinal cord, with age-related cognitive dysfunctions, particularly in Alzheimer's disease (AD) strongly associated with neurotransmission abnormalities. Aluminium (Al), the third most abundant metal in the Earth's crust, is recognized for its neurotoxic properties, while D-galactose (D-gal), a reducing sugar, induces cellular senescence through its interaction with amino acid residues in proteins. The combined administration of Al and D-gal has been established as a model for inducing neurotoxicity and studying AD mechanisms. Virgin Coconut Oil (VCO), a natural supplement rich in medium-chain triglycerides convertible to ketone bodies for cerebral energy metabolism, has demonstrated potential in promoting neurogenesis in aging models. This study investigates the neuroprotective effects of VCO in a rat model of cognitive dysfunction induced by Aluminium Chloride ($AlCl_3$) and D-gal. Thirty-five healthy male albino Wistar rats (150–200 g) were administered D-gal (60 mg/kg, intraperitoneally) and $AlCl_3$ (200 mg/kg,

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orally). Rats in treatment groups received VCO at doses of 1 and 3 ml/kg/day, while a positive control group was treated with donepezil (1 mg/kg) alongside $AlCl_3$ and D-gal. Cognitive performance was assessed using the Novel Object Recognition test; oxidative stress was evaluated by measuring hippocampal malondialdehyde (MDA) levels, and histological analysis of the CA1 region was conducted to assess neuronal integrity. Rats exposed to $AlCl_3$ and D-gal exhibited significant cognitive deficits, elevated MDA levels, and hippocampal neuronal loss ($p < 0.05$). VCO administration significantly attenuated these impairments by reducing oxidative stress and preserving hippocampal cytoarchitecture. These findings suggest that VCO possesses neurotherapeutic potential for mitigating AD-related cognitive impairments.

Keywords: Virgin Coconut Oil; Cognitive Function; Aluminium Chloride; D-galactose; Alzheimer's disease; Oxidative Stress; Neurogenesis

INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that causes problems with memory, thinking and behavior, it is caused by damage to the brain nerve cells which are essential for thinking, walking, talking and all human activities. Alzheimer's disease is the most common cause of dementia, accounting for 60% to 80% of dementia cases (Henderson, 2023).

AD has also been described as a slowly progressive neurodegenerative disease characterized by impaired personal daily activities and other symptoms like aphasia (impairment of a language), apraxia (a motor skills disorder), and agnosia (a loss of perception) (Bereijyeh and Karaman, 2020). AD is not a normal part of aging, and it is the most common cause of dementia in most people of age 65 and beyond, accounting for 60% to 80% of dementia cases worldwide (Bekhedda *et al.,* 2020).

Two main types of AD have been established and these include; early-onset AD which affects people less than 65 years of age, and late-onset AD, which affects people older than 65 years (Mahdi *et al*., 2021). Due to the progressive nature of the disease, and the clinical symptoms continue to rise with increase in age. AD has been classified based on the severity of its clinical symptoms into, mild, moderate and severe stages (Mahdi *et al*., and Henderson, 2023). In all the types of AD highlighted, the hippocampus and cerebral cortex

are the most preferentially and severely affected parts of the brain in AD (Henderson, 2023).

As of 2020, there are around 50 million AD patients worldwide and this number is projected to double every 5 years and will increase to reach 152 million by 2050 (Breijyeh and Karaman, 2020). The key pathological hallmarks of AD are the accumulation of senile plaques due to the aggregation of the extracellular protein fragment β-amyloid (Aβ) and the formation of intracellular neurofibrillary tau tangles (NFT) of tau proteins and synaptic loss (Sandupama, et al., 2022; Breijyeh and Karaman, 2020). AD is also characterized by the loss of cholinergic neurons in the basal forebrain in humans (Mahdi et al., 2021).

AD is also characterized with loss of acetylcholine, oxidative damage, mitochondrial dysfunction, neuroinflammation and amyloid plaques accumulation with hyper phosphorylated tau protein in the brain (Du et al., 2018) However, recent research has shown that the underlying etiology of AD has also been linked to metabolic diseases including brain insulin resistance, which results in neuronal death (Wood, 2017)). More importantly, such pathologies may progress gradually over decades before the first signs of the disease appear (Jack et al., 2013). Interestingly, hippocampal neurogenesis is also impaired before typical AD symptoms appear (Mu and Gage, 2011).

Aluminium (Al) is the third most abundant metal that constitutes about 8% of the total earth crust (Laabbar et al., 2014). Humans get exposed to Al through cooking utensils, food, antacids and deodorants, beside occupational exposure such as defense related factories, automobiles and guns (Singh and Goel, 2015). Al compounds can reach the systematic circulation via different routes such as by dermal absorption, ingestion and intramuscular injection (Laabbar et al., 2013).

Recently, research on animals and clinical studies has indicated that Al has significant toxic effects on the central nervous system, particularly impacting cognitive functions. These effects are attributed to neuropathological changes induced by Al, highlighting its potent neurotoxicity (Sood et al., 2011).

Several studies have reported the effects of Al on altering the blood brain barrier (BBB) and get easy access into the brain under normal physiological states and further accumulate in various regions of the brain (Kakkar and Kaur, 2011). Further recent reports suggested the involvement of Al in elevation of oxidative and inflammatory stress markers which

result in disruption of intraneuronal metal homeostasis along with axonal transport and long-term potentiation disruption (Singh and Goel, 2015).

Al enters brain enters the brain through transferrin receptors expressed in the BBB but cannot exit, leading to gradual accumulation in the brain gradually increases with age (Walton, 2012). Previous research strongly links Al accumulation in brain and progression of AD-like symptoms such as aggregation of hyper phosphorylated tau-protein which consists of neurofibrillary tangles (NFTs) and accumulation of insoluble amyloid-β (Aβ) proteins as Aβ plaques (Yumoto et al., 2009). NFTs and Aβ plaques are well established in AD patients and are mainly responsible for distinctive signs and symptoms observed in AD including cognitive dysfunction (Thenmozhi, 2015) psychological disturbance and impaired neurotransmission (Laabbar et al., 2014). Elevated Al levels have also been reported as a factor in some less common neurological disorders such as Parkinsonian-ALS (Bondy, 2010).

D-gal is a known type of sugar that reacts with the free amines of amino acids in proteins, it has been identified as a contributor to ageing generating advanced glycation end products (AGEs) (Mahdi et al., 2021). Prolonged chronic administration of D-gal at low doses induces changes in rats resembling natural ageing process including oxidative stress, cognitive decline, weakened immune response, and alterations in gene transcription. Chronic exposure to D-gal has been used to simulate neurotoxicity providing a model for studying the mechanism of AD. Furthermore, the combination of AlCl3 and D-gal creates a model for AD-like pathologies and cognitive impairments, facilitating research on potential AD therapies (Mahdi et al., 2021 and Muaz and Nilsel, 2023).

Coconut Oil have in recent studies reported to have neuroprotective effect against AD pathogenesis by enhancing the survival of cortical neurons exposed to Aβ and suppressing the mitochondrial alterations induced by Aβ (Nafar et al., 2017 & Nafar and Mearow, 2014) increase plasma ketone body (βHB) concentrations (Reger et al., 2004 and Taylor et al., 2018), enhancing synaptic transmission, and cholinergic function (Muaz and Nilsel, 2023). Coconut oil one of the prominent foods that is strongly linked to healthy brain function is coconut oil (Muaz and Nilsel, 2023). It is produced from coconut fruit (*Cocos nucifera* L., family Arecaceae) an important fruit tree in the world. Coconut oil is one of the most important edible oils for domestic use, the oil is rich in high proportion of medium chain triglycerides (MCT) of lower chain fatty acids usually medium chain fatty acids

(MCFA) and exhibits good digestibility (Shahidi, 2006 and Krishna A.G *et al*., 2010).The oil is highly stable towards atmospheric oxidation and is characterized by a low iodine value, high saponification value, high saturated fatty acids content and is liquid at room temperatures of 27°C (Krishna *et al.,* 2010).

VCO has also been proposed to have therapeutic effect in AD pathogenesis by targeting oxidative stress. In cell culture studies (HCT-15 cells), VCO polyphenol pre-treatment was found to reduce oxidant-induced oxidative stress and cell death, restoring to near-normal the levels of glutathione, as well as glutathione reductase, glutathione peroxidase and catalase activities in the cells (Illam et al., 2017). Several studies have indicated that VCO derivatives can improve cognition. For example, in mild-moderate AD patients, the oral intake of Medium Chain Triglycerides (MCT) for three months resulted in increased plasma ketone body (βHB) concentrations, which was associated positively with cognitive performance. (Reger *et al.,* 2004 and Taylor *et al*., 2018). There have not been sufficient studies on the neuroprotective effect of coconut oil in mitigating neurodegenerative disorders like Alzheimer's disease. Thus, this research aims to assess the neuroprotective effect of coconut oil on $AlCl_3$ and D-gal induced cognitive impairment, and possibly provide a natural remedy for the neurodegenerative diseases. VCO, a natural supplement rich in medium chain triglycerides which can be converted into Ketones and be utilized by the brain in absence of glucose, could attenuates cognitive impairment induced by $AlCl_3$ and D-gal.

MATERIALS AND METHODS

Animals

Thirty-five (35) healthy albino male Wistar rats weighing between 150-200g were sourced from the animal facility from the Department of Human Anatomy, University of Jos. These rats were housed in cages within a temperature-controlled environment with 12-hour alternating cycles. The rats had access to unlimited water and were fed with a standard diet on a regular basis. Ethical approval was obtained from the ethical committee for the care and handling of laboratory animals of the College of Basic Medical Sciences Gombe State University, and rats were handled in humane manner according to the approved animal experimental procedures.

Plant Extract and Chemicals

D-gal (cat no.:886321) and $AlCl_3$ (cat no.:14600) were free donations from the Department of Biochemistry and the Faculty of Pharmaceutical Sciences respectively. While VCO was extracted using the cold and pressing method according to Nevin and Rajamohan, 2004. Mature coconuts were purchased from commercial sellers in Gombe main market and were used for the extraction of VCO. D-gal was dissolved in distilled water for intraperitoneal (i.p.) injection, $AlCl_3$ was dissolved in distilled water for oral delivery (using oral gavage) and VCO was administered orally without dilution using oral gavage.

Experimental Design

Following one week of acclimatization, thirty-five (35) male albino Wistar rats were randomly divided to five (5) groups, of seven (7) rats each; the control group (feed and distilled water), the model group ($AlCl_3$ 200 mg/kg/orally/day + D-gal 60 mg/kg/i.p./day) adapted from Mahdi et al., 2021, the Donepezil group (Model + Donepezil 1mg/kg/orally/day) as adapted from Song et al., 2017, the low VCO group (Model + VCO 1 ml/kg/orally/day) and the high VCO group (Model + VCO 3 ml/kg/orally/day). The dosage of VCO was selected based on the research on Muaz and Nssil, 2023. Donepezil is used for symptomatic treatment of AD. Thus, the donepezil administered group serves as a positive control group in this study in order to compare its effects to VCO. Body weight of the rats was measured in first week of the experiment, before starting administration and in the last week of the experiment.

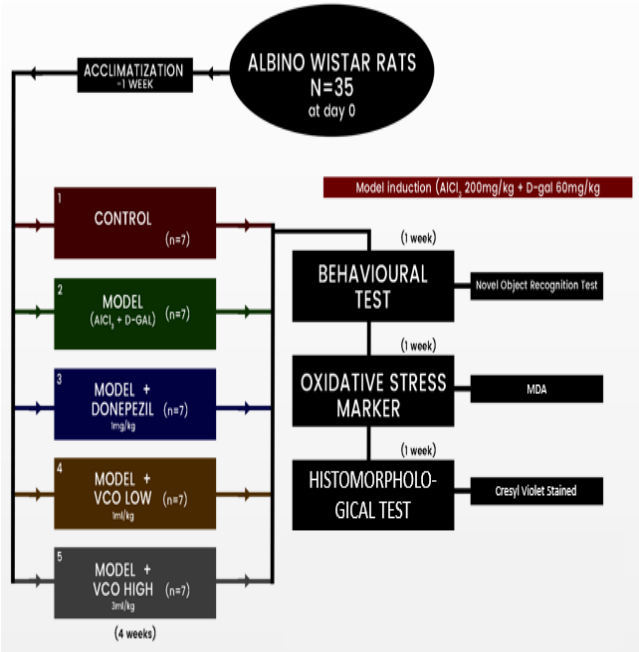


Figure 1. Experimental design to test rat's cognitive function, check the level of damage on the hippocampus and quantify oxidative stress and neurogenesis markers following the induction of cognitive impairments by $AlCl_3$ and D-gal co-administered with VCO. SOD - superoxide dismutase, MDA - Malonaldehyde, Model = $AlCl_3$ + D-gal, $AlCl_3$ - Aluminium chloride, D-gal—D-galactose, VCO - Virgin coconut oil.

Novel Object Recognition (NOR)

The Novel Object Recognition (NOR) test is a widely used behavioral assay used to assess recognition memory in rats in neuroscience research. This test relies on the innate preference of rats for exploring novel objects over familiar ones. Rats are allowed to freely explore the environment having two identical objects for a set period during the training phase. Following the training phase, one of the familiar objects was replaced with a novel object (Antunes and Biala, 2012).

The same environment was reintroduced to the rats but now with one familiar object and one novel object. The NOR test relies on the principle that if the rat remembers the familiar object from the training phase, it will spend more time exploring the novel object during the test phase (Antunes and Biala, 2012). The measure of recognition memory performance is carried out using the ratio of time spent exploring the novel object compared to the familiar object.

Sample Collection and Preparation

Following the euthanasia, the brain tissues were harvested and immersed in saline solution. After being rinsed, the tissues for histological studies were cleaned with normal saline and immediately deposited in a 10% formalin solution. The brain samples were then processed for histological observations. Hippocampal samples were extracted from the rats' brains and stained using Nissl stain. The entire brains were removed and fixed in 10% neutral buffered formalin. These fixed brain tissues were placed in tissue cassettes and dehydrated with an automated tissue processor. The processed brain tissues were then embedded in paraffin blocks using an embedding machine. Using a microtome, coronal sections of the tissue blocks were cut, forming continuous ribbons of tissue sections. These ribbons were carefully collected and floated in a water bath to straighten the sections before placing them on glass slides. The tissues were then deparaffinized in xylene and rehydrated in graded alcohol for 3 minutes at each concentration, followed by a final rinse in distilled water for 3

minutes. The tissue sections were stained with cresyl violet acetate solution to evaluate neuronal damage in the rats' brains. The slides were subsequently washed in distilled water for 3 minutes and dehydrated in graded alcohol for 3 minutes at each concentration. After dehydration, the tissues were placed in xylene for 5 minutes before being mounted and covered with a cover slip. Images were captured using a Motic™ compound light microscope.

Measurements of Biochemical and Neurogenesis Parameters

The levels of MDA were measured in the blood sample tissues because oxidative stress and the antioxidant defense system are crucial in the pathophysiology of AD. These tests were carried out in the laboratory of Biochemistry Department, Gombe State University.

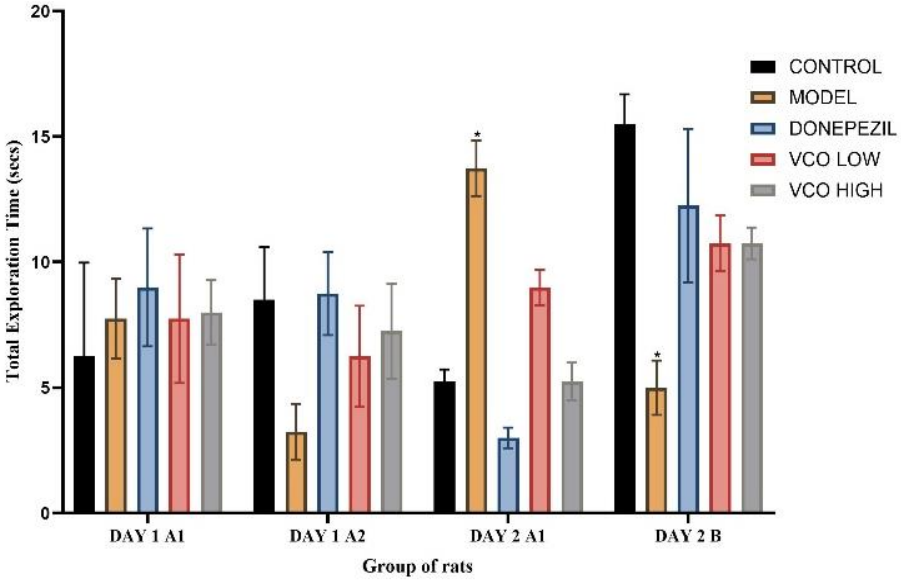
RESULTS

VCO Attenuates $AlCl_3$ and D-gal Induced Cognitive Impairments in Rats during Novel Object Recognition (NOR) Test

The NOR test was conducted to see how effective VCO was at improving cognitive impairment in rats caused by $AlCl_3$ and D-gal. Figure 2 showed a graph of the time the different rat groups spent exploring the familiar objects versus the novel object during familiarization and testing. Normally rats spend more time with the familiar object, showing preference. This indicates learning and memory. However, the model group of rats spent a similar less time on both objects, showing memory loss. Two-way ANOVA indicated statistically significant differences in the interactions between the time spent on the two different objects, [$F(4, 15) = 23.26$, $p < 0.05$]. Tukey's post hoc comparison revealed statistically significant difference decreases ($p < 0.05$) in the time spent on the two different objects by the model group, donepezil, VCO low dose and VCO high dose rats' groups in comparison with the control. Furthermore, One-way ANOVA [$F(4, 15) = 33.20$, $p<0.05$] exhibited statistically significant differences in the times spent on the familiar object by the various rat groups. Tukey's multiple comparisons test indicated statistically significant difference decreases in the times spent on the familiar object by the control (5.250 ± 0.4787, $p<0.001$), donepezil (3.000 ± 0.4082, $p<0.001$), VCO low dose (9.000 ± 0.7071, $p<0.001$) and VCO high dose (5.250 ± 0.7500, $p<0.001$) rat's groups in comparison with the model group ($13.75 \pm$

1.109, p<0.001).

Also, one-way ANOVA [F (4, 15) = 5.313, p=0.0072] exhibited statistically significant differences in the times spent on the Novel object by the various rat groups. Tukey's multiple comparisons test indicated statistically significant different increases in the times spent on the novel object by the control (15.50 ± 1.190, p<0.001), donepezil (12.25 ± 3.065, p<0.001), VCO low dose (10.75 ± 1.109, p<0.001) and VCO high dose (10.75 ± 0.6292, p<0.001) rats' groups in comparison with the model group (5.000 ± 1.080, p<0.001).



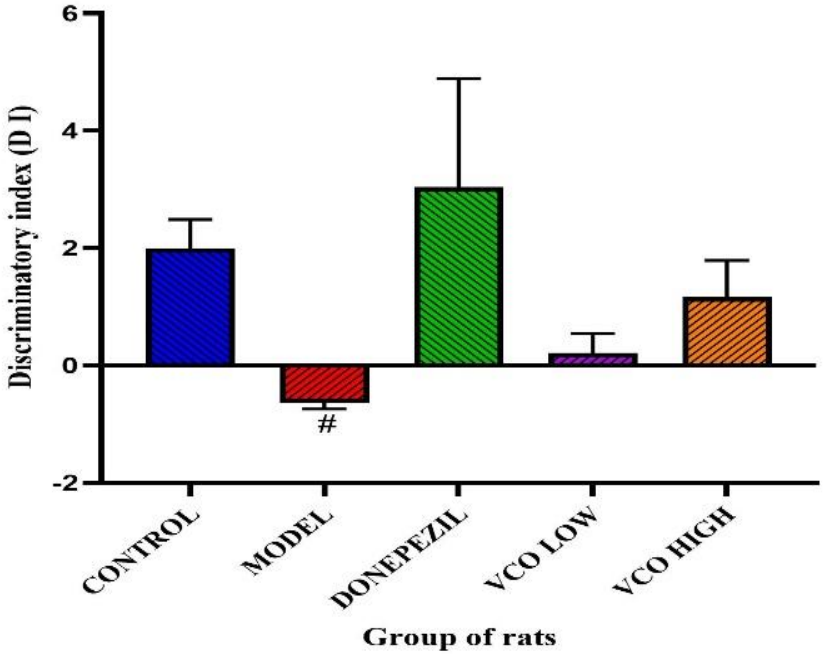


Figure 2A: Assessment of spatial learning and memory of rats in Novel Object Recognition test. Time spent on both Familiarized and Novel object. The experimental groups include; Normal saline + Distilled water (control), Model ($AlCl_3$ 200 mg/kg + D-gal 60 mg/kg), positive control (Model + Donepezil 1mg/kg) VCO low (Model + VCO 1ml/kg) and VCO high (Model + VCO 2ml/kg). Data were expressed as mean ± SEM, (n=4). Statistical analysis was performed by two-way repeated measures ANOVA. A1 and A2 represent familiar objects, B represent Novel object. **2B** Indicates the discrimination index (DI) of the rats towards the novel object which was calculated by subtracting the time spent on the novel object from the time spent on the familiar object and was divided by the time spent on the familiar object. The DI shows the level of preference for the novel object between the groups. One-way ANOVA at $p<0.05$, n=4.

Histological Findings

Upon observation of the brain morphology, neuronal loss was evident in the model group, whereas the control group's brain structure remained intact (Figure 3). Micrographs of the control groups showed a compact layer of pyramidal cells with clear nuclei (indicated with black arrows), signifying healthy neurons. Obvious changes were seen in the pyramidal cell layer and degenerating neurons (as seen by darkly stained cells indicated with a red arrow head) in the CA1 region of the model group. Whereas the treatment group exhibited a dense layer of pyramidal cells with clear nuclei like the control group, indicating the presence of healthy cells. The Control, CA1-CA4 image showed the entire hippocampus at 10x magnification. At x40, the Control, CA1 image revealed a dense layer of normal pyramidal cells. The Model, CA1 slide indicated degenerated pyramidal cells and disrupted layer arrangement (indicated using a red arrow head). Donepezil, CA1 showed a thinned pyramidal layer with some degraded cells. The high dose VCO group had an abundance of normal pyramidal cells like the control. The low dose VCO group displayed fewer pyramidal cells, suggesting alterations. Black arrows pointed to viable neurons while red denoted dead neurons.

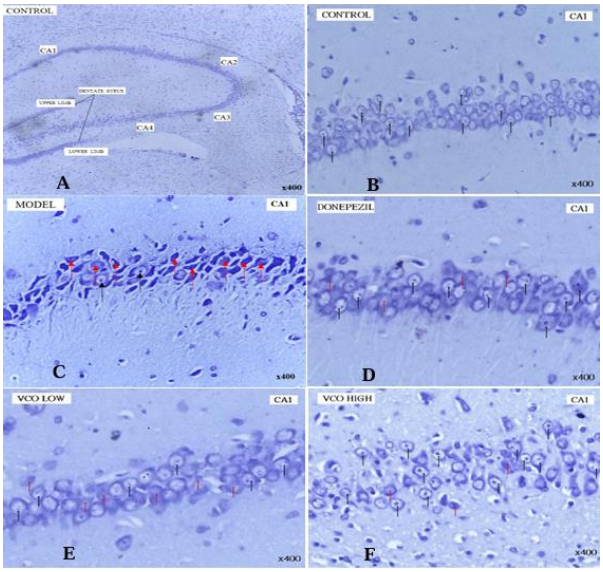


Figure 3A: Full section of hippocampus from group one (1) control group showing: CA = Cornu Ammonis, and magnification – x40. **B**; CA1 showing more life cell present with a nucleus located in the center as showed by the arrows, x400. **C**; CA1 from the Model group: the red arrows are pointing at dead cells with abnormal morphology and cells stalking on each other. The black arrows are pointing at the normal cells in the hippocampal cells, x400. **D**; CA1 showed a thinned pyramidal layer with some degraded cells. The features of the neuronal cells in this group are close to that of the control group of rats, x400. **E**; The low dose VCO group displayed fewer pyramidal cells, signifying alterations. Black arrows pointed to viable neurons while red indicated dead neurons, x400. **F**; The high dose VCO group had shown an abundance of normal pyramidal cells like the control compared to the number of abnormal cells. Stain: Cresyl violet (Nissl stain).

Biochemical Findings

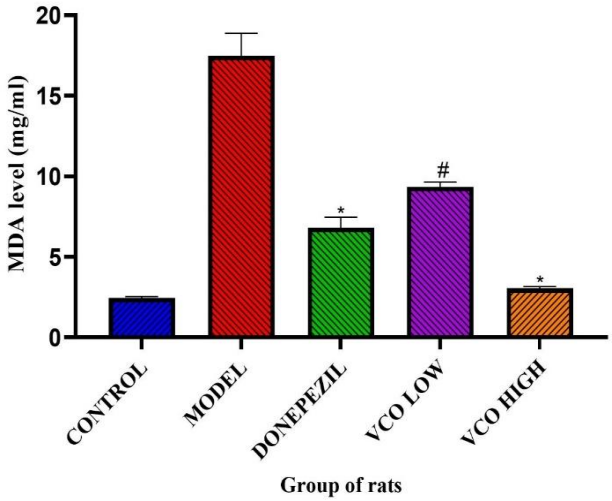


Figure 4: Effects of VCO on MDA activities in the brains of D-gal and $AlCl_3$ induced rats. Values are shown as mean ± SEM, n = 4. A significant statistical difference ($p<0.05$) was observed in the MDA level in all the groups except for VCO high compared to the control group [F (4, 15) = 74.43, P<0.0001]. Turkeys post hoc test for multiple comparison further revealed that there was a significant statistical difference in the MDA level between the model group and the control group [F (4, 15) = 74.43, P<0.0001], a significant statistical difference was also observed between the control group and the low dose VCO treated group [F (4, 15) = 74.43, P<0.0001]. However, less significant statistical difference was observed between the control group and high dose VCO treated groups [F (4, 15) = 74.43, P = 0.9735]. VCO – Virgin Coconut oil, MDA – Malondialdehyde.

Higher levels of MDA are one of the known pointers of oxidative damage in the brains of rats, and MDA levels were quantified in the rat brains. The model rat groups displayed a significant increase in the MDA levels in the brain when compared to the control, donepezil and the WIN co-administered groups of rats. One-way ANOVA showed statistically significant differences in MDA levels in the brain of the rats [F (4, 15) = 74.43, $p < 0.05$]. Tukey's post hoc showed statistically significant different increases of MDA levels in the brain of the model group of rats (17.48 ± 1.401, p <0.0001), in contrast to the control group (2.458 ± 0.08882, p<0.001). Treatment of rats with donepezil 1mg/kg/day reduced MDA levels (6.815 ± 0.6431, p = 0.0043) in their brains. Additionally, MDA levels in D-gal and $A1Cl_3$-induced rats were decreased by the treatment with VCO low (9.350 ± 0.3031, p <0.0001) and VCO high (3.053 ± 0.1149, p <0.)001) in comparison with the model group of rats (17.48 ± 1.401, p <0.0001.

DISCUSSION

The results of this study provide valuable insights into the effectiveness of different treatments in improving cognitive function in rats with induced cognitive impairment using virgin coconut oil. The comparative analysis of the groups reveals interesting findings.

To begin with, the control group serves as a baseline for normal cognitive function, demonstrating that the induction of cognitive impairment in the other groups was successful. This ensures the validity of the model used in the experiment. The model group, which received $AlCl_3$ and D-galactose, exhibited significant cognitive impairment

compared to the control group. This validates the efficacy of the model in inducing cognitive impairment in the rats as seen in Mahdi *et al.*, (2021).

The group treated with Donepezil, a known cognitive enhancer, showed notable improvement in cognitive function. This finding aligns with previous research on the therapeutic effects of Donepezil in mitigating cognitive impairment (Montero-Odasso *et al.*, 2018). The positive outcome in this group serves as a benchmark for the effectiveness of interventions in improving cognitive function.

Interestingly, both the high-dose VCO group and the low-dose VCO group exhibited improvements in cognitive function, although to varying degrees. The high-dose VCO group demonstrated significant improvement, comparable to the group treated with Donepezil. This suggests that high-dose VCO treatment has neuroprotective effect on cognitive impairment as Donepezil.

On the other hand, the low-dose VCO group showed a modest improvement in cognitive function. While the improvement was not as substantial as in the high-dose VCO group or the Donepezil group, it is still noteworthy. This indicates that even a lower dosage of VCO has the potential to offer some cognitive benefits. These findings suggest that VCO, particularly at higher doses, has the potential to improve cognitive function in rats with induced cognitive impairment. The results aligned with previous studies highlighting the potential neuroprotective and cognitive-enhancing effects of VCO due to its antioxidant and anti-inflammatory properties (Muaz & Nilsel, 2023).

In this study, the model group induced with $AlCl_3$ and D-gal exhibited a significant decline in cognitive performance compared to the control group. This impairment is consistent with previous research that has established the cognitive-disruptive effects of $AlCl_3$ and D-gal (Mahdi *et al.*, 2021). However, the administration of VCO showed promising results in attenuating cognitive impairment. The high-dose VCO group demonstrated significant improvement in cognitive function, comparable to the group treated with Donepezil. This suggests that VCO may possess cognitive-enhancing properties, potentially mitigating the effects of $AlCl_3$ and D-gal.

The model group exhibited elevated levels of MDA, suggesting increased oxidative stress in the brain. However, treatment with VCO led to a significant reduction in MDA levels, indicating its potential as an antioxidant agent. The reduction in oxidative stress markers is consistent with previous research on the neuroprotective effects of VCO's antioxidant

compounds, such as phenolic acids and tocopherols (Muaz and Nilsel, 2023). These compounds may scavenge free radicals, protect cellular structures from oxidative damage, and contribute to the preservation of cognitive function.

The assessment of vitamin A and iron levels revealed interesting findings. The model group exhibited decreased vitamin A levels compared to the control group, suggesting an alteration in vitamin A management induced by $AlCl_3$ and D-gal. However, treatment with high-dose VCO resulted in a significant increase in vitamin A levels, potentially indicating a role for VCO in maintaining adequate vitamin A levels and enhancing cognitive function. Iron levels were also modulated by VCO treatment, with the high-dose group showing an increase compared to the model group. Iron dysregulation has been implicated in neurodegenerative diseases, and the ability of VCO to modulate iron levels may contribute to its neuroprotective effects.

The biochemical assessments provide valuable insights into the potential mechanisms underlying the cognitive benefits of VCO. By reducing oxidative stress (Rahim *et al.*, 2017), enhancing antioxidant activity (Zeng *et al.*, 2022), and modulating essential micronutrients, VCO may contribute to the protection of neuronal cells and the preservation of cognitive function just as seen in the anchor paper of this research (Muaz and Nilsel, 2023).

The histomorphological findings complement the behavioral and biochemical assessments, providing additional evidence for the beneficial effects of VCO on cognitive impairment. The potential of VCO to improve neuronal integrity further supports its potential as a neuroprotective intervention for cognitive impairment.

CONCLUSION

In conclusion, this research has provided invaluable insights into the neuroprotective effect of VCO on cognitive impairment induced by $AlCl_3$ and D-gal in rats. The findings demonstrate that VCO, particularly at high doses, showed significant improvement in cognitive function, comparable to the effects seen in Donepezil group. Even at lower doses, VCO exhibits modest improvements in cognitive function.

Nevertheless, it is important to acknowledge the limitations of this study. The research was conducted on rats, and further studies are needed to determine the applicability of these

findings on other species. Furthermore, the optimal dosage and duration of VCO treatment require further investigation to maximize its neuroprotective ability.

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Declaration of Conflicts of Interests

Authors have declared that there is no conflict of interest.

Abbreviations

Aβ	Amyloid beta
Aβ42	Amyloid beta 42
AD	Alzheimer's disease
AGES	Advanced glycation end products
Al	Aluminium
$AlCl_3$	Aluminium chloride
ANOVA	Analysis of variance
BBB	Blood brain barrier
CA1–4	Connus ammonis 1–4
D-gal	D-galactose
IP	Intraperitoneal
MCFA	Medium chain fatty acids
MCT	Medium Chain Triglycerides
MDA	Malonaldehyde
n	Number of rats per group
NFT	Neurofibrillary tau tangles
NOR	Novel object recognition
SEM	Standard error of mean
SOD	Superoxide dismutase
VCO	Virgin coconut oil

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