

## Effect of ethanol leaf extract and fractions of *Launaea taraxacifolia* on cognimotor and visuospatial functions in aluminium chloride neurotoxic rats

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### Abstract

Aluminium chloride neurotoxicity is a well-established model of neurodegeneration. This study investigated the potential neuroprotective effects of ethanol leaf extract and fractions of *Launaea taraxacifolia* (*L. taraxacifolia*) on cognitive and motor functions in aluminium chloride-treated rats. Sixty-six adult female Wistar rats were divided into 11 groups. The neurotoxic control group received aluminium chloride (100 mg/kg), while experimental groups received additional treatments, including donepezil, ethanol extract (274 – 822 mg/kg), and various solvent fractions for 21 days. Neurobehavioral tests (wire hang test, beam walking test, T-maze, and novel object recognition) assessed motor coordination and cognition. Aluminium chloride exposure significantly impaired hanging time, increased foot slips and crossing time, reduced percentage alternation in the T-maze, and decreased novel object exploration ( $p < 0.05$ ). Treatment with *L. taraxacifolia* extract and fractions significantly improved all these parameters ( $p < 0.05$ ), indicating enhanced motor coordination, cognitive flexibility, and visuospatial function. These findings suggest that ethanol leaf extract and fractions of *L. taraxacifolia* possess neuroprotective properties, mitigating aluminium chloride-induced neurotoxicity and improving cognitive and motor performance in rats.

**Keywords:** Ethanol extract, *Launaea taraxacifolia*, aluminium chloride neurotoxicity, Cognimotor, visuospatial functions.

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### 1. Introduction

Aluminium is a neurotoxic element implicated in several neurochemical, neuropathological, electrophysiological, and behavioural changes associated with cognitive impairment (Wang, 2018). Neurotoxic properties of aluminium exposure depend on several factors including dose, duration, and route of exposure, chemical forms, metabolism, detoxification and distribution, and elimination. (Ljiljana *et al.*, 2022). Cognitive decline can be behaviourally tested on sensory, motor, and learning abilities. The behavioural tests in animals include visual,

motor, sensorimotor, gross motor, and fine motor performances and reflexes, coordination and locomotion (Ljiljana *et al.*, 2022).

Acute exposure to aluminium can cause clinical neurotoxicity. Aluminium in vaccines can cause neuroinflammation, cell loss and memory deficit (Petrik *et al.*, 2007). Sporadic cases include seizure disorder, ataxia, and dysarthria. Aluminium levels in the brain are increasing with age, which may lead to neurodegenerative diseases. Alzheimer's disease and Parkinson's disease are the most common aluminium – related diseases. Alzheimer's disease (AD) develops in the area where the aluminium concentration in drinking water is higher, and the main symptoms are dementia, development of amyloid plaques consisting of aggregated  $\beta$ -amyloid proteins and neurofibrillary tangles consisting of aggregated tau proteins, production of reactive oxygen species, reactive microglia, and the production of pro-inflammatory cytokines and macrophage activity (Polizzi *et al.*, 2016). Aluminium exposure may induce the disorder in dopamine related brain regions, mostly the striatum, and together with inflammation and microglial activation lead to Parkinson's disease (Petrik *et al.*, 2007). An increasing body of evidence implicates aluminium in the progression of events that lead to dementia and neurodegenerative diseases (Petrik *et al.*, 2007). It is accepted that aluminium is a recognized neurotoxin that could cause neurodegenerative diseases such as Alzheimer's disease (Petrik *et al.*, 2007). The pathological changes induced in aluminium neurotoxicity leading to Alzheimer's disease result in critical impairments of the central nervous system functions, which are essential for healthy brain aging. These changes include axonal transport, neurotransmitter synthesis and synaptic transmission, alteration of energy metabolism, phosphorylation/dephosphorylation of proteins, inhibition of DNA repair system, activation of glial cells, protein degradation, gene expression, formation of reactive oxygen species and inflammatory responses, reduction of activities of antioxidant enzymes, binding DNA, motor and cognitive decline (Chiroma *et al.*, 2019). These multi-faceted pathways provide a link between aluminium neurotoxicity and Alzheimer's disease by modulating both tau and amyloid beta hypothesis of Alzheimer's disease (Exley, 2013).

A novel investigation focused on the mechanisms of neuroprotection and many substances have been tested on animal models of diseases but potential drugs have not yet been found. Currently, many researchers have resorted to plant as possible source for obtaining novel bioactive agents in combating these disorders. The leaves of *L. taraxacifolia* are endowed with saponins, terpenoids, cardiac glycosides, steroids, tannins, flavonoids, leucoanthocyanins, phenolic acids, ascorbic acid, lycopene and  $\beta$ -carotene (Adinortey *et al.*, 2014). Ololade *et al.*, (2017) have isolated 47 compounds from methanolic extract of the *L. taraxacifolia* leaves. The most abundant chemical components found were palmitic acid, methyl-11-octadecenoate, erythritol, glycerol, linoleic acid methyl ester, and phytol.

Research over the years has revealed that *L. taraxacifolia* possess important pharmacological activities (Adinortey *et al.*, 2014). Studies have demonstrated that *L. taraxacifolia* leaf extract has antioxidant power to protect against oxidative stress. The phytochemical screening of *L. taraxacifolia* conducted by Anyanwu *et al.*, (2022) revealed that the plant is rich in alkaloids, tannins, flavonoids, saponins, phenols, steroids, cardiac glycosides and terpenoids, which are common chemical constituents of many traditionally prepared herbal medicines and leafy vegetables.

## 2. Materials and Methods

### 2.1 Drugs and chemicals

All the drug solutions were freshly prepared before use. Donepezil (Donepezil Hydrochloride Tablet USP, Smick Laboratories Ltd., Batch No: T7638, 5 mg) an acetyl cholinesterase inhibitor was purchased from a reputable pharmaceutical company (Tibest Pharmacy) located at No. 28 Calabar – Itu Highway, Itam, Uyo, Akwa Ibom State. Aluminium chloride ( $AlCl_3$ ) was purchased from Mike Ene Scientific/Chemicals Company Limited located at No. 41, Udi Street, Uyo, Akwa Ibom State. The polar and non-polar agents (ethanol, n-hexane, dichloromethane, ethyl acetate and n-butanol) were acquired from the Department of Pharmacognosy and

Natural Medicine, Faculty of Pharmacy, University of Uyo, Uyo, Akwa Ibom State. All the reagents used in this study were of analytical grade.

## 2.2 Collection of identification and authentication of plant material

*Launaea taraxacifolia* was collected from the laboratory environment of the Department of Pharmacognosy and Natural Medicine, University of Uyo, Uyo, Akwa Ibom State. It was identified, and the specimen with Voucher No: UUPH 10 (P) was deposited in the Herbarium, Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo, Uyo, Akwa Ibom State.

## 2.3 Preparation of the Extract of Plant Material

The leaves of *L. taraxacifolia* were collected, washed, cut into small pieces, and dried in open air in the laboratory. The dried leaves were pulverized into coarse powder using mortar and pestle. The powdered plant material was weighed and transferred into a transparent airtight container prior to extraction. Thereafter, 740 g of pulverized leaves was extracted by maceration in 4L of 70 % ethanol. The mixture was shaken time to time to ensure complete extraction of the plant's bioactive ingredients. The mixture was separated by filtration using Whatman filter paper size 1. The filtrate was concentrated to dryness in a water bath (Grant GLS400, Model No. 8T0902004, England) at 45 °C. The ethanol extract of *L. taraxacifolia* was weighed (using the Mettler Toledo electronic scale; model no. P103, Italy) and stored in a deep freezer at -4 °C.

## 2.4 Partitioning of Ethanol Extract of *L. taraxacifolia*

Ethanol extract (136 g) was partitioned successively into five solvent fractions by separating funnel starting from n-hexane, dichloromethane (DCM), ethyl acetate and n-butanol. The solution was continually stirred and decanted until clear supernatant was obtained. The fractions were concentrated using a rotary evaporator (Model No. R-205, England) at 40 °C. The concentrated fractions were transferred into small beakers (50 mL) and further concentrated in a water bath (Grant GLS400, Model No. 8T0902004, England) at 45 °C to ensure that all the solvents that were used during partitioning were removed. The fractions were refrigerated at 4 °C until needed.

## 2.5 Experimental Design

Prior to the start of the experiment, the animals were randomly divided into eleven groups of 6 rats each and treated for 21 days as shown in **Table 1**.

## 2.6 Visuospatial Functions (Memory Test)

The effect of ethanol extract and fractions of *L. taraxacifolia* on visuospatial functions were evaluated using T-maze simple alternation test and novel object recognition test (NORT). Memory test was carried out after day 21 of treatment.

## 2.7 T-Maze Simple Alternation Test

*Procedure:* The maze was set so that the central partition was in place. The animal was placed in the start area and allowed to choose a goal arm. After each alternation (30 seconds), the animal was returned to the maze for another alternation test. Each animal was subjected to 5 pair different trial making a total of 10 trials. With each pair of trial, the animal was determined to have passed or failed. Any animal that repeats a particular alternation (picked the same arm) in a pair of trial was considered to have failed the trial, while the animal that picked alternate arm in a single pair was considered to have passed the trial. At the end of the trial, the percentage (%) alternation was calculated for each animal. Percentage (%) alternation was calculated thus:

$$\frac{\text{Number of phases with good alternation} \times 100}{\text{Total Number of phases}}$$

**Table 1.** Method of AlCl<sub>3</sub> Neurotoxicity in Rats

S/N	Group	Treatment	Duration of Treatment
1.	Control	10 mg/kg body weight of distilled water	Daily for 21 days
2.	AlCl <sub>3</sub> (Neurotoxic Control)	100mg/kg body weight of AlCl <sub>3</sub>	Daily for 21 days
3.	AlCl <sub>3</sub> +Donepezil	100 mg/kg body weight of AlCl <sub>3</sub> and 2.5 mg/kg body weight of Donepezil	Daily for 21 days
4.	AlCl <sub>3</sub> + Ethanol extract (LD)	100mg/kg body weight of AlCl <sub>3</sub> and 274mg/kg body weight of ethanol extract (Low dose) of <i>L. taraxacifolia</i>	Daily for 21 days
5.	AlCl <sub>3</sub> + Ethanol extract (MD)	100mg/kg body weight of AlCl <sub>3</sub> and 548mg/kg body weight of ethanol extract (Middle dose) of <i>L. taraxacifolia</i>	Daily for 21 days
6.	AlCl <sub>3</sub> + Ethanol extract (HD)	100 mg/kg body weight of AlCl <sub>3</sub> and 822mg/kg body weight of ethanol extract (High dose) of <i>L. taraxacifolia</i> .	Daily for 21 days
7.	AlCl <sub>3</sub> + N-hexane fraction	100 mg/kg body weight of AlCl <sub>3</sub> and 548mg/kg body of n-hexane fraction of <i>L. taraxacifolia</i>	Daily for 21 days
8.	AlCl <sub>3</sub> + DCM fraction	100 mg/kg body weight of AlCl <sub>3</sub> and 548mg/kg body weight of DCM fraction of <i>L. taraxacifolia</i> .	Daily for 21 days
9.	AlCl <sub>3</sub> + Ethyl acetate fraction	100 mg/kg body weight of AlCl <sub>3</sub> and 548mg/kg body weight of ethyl acetate fraction of <i>L. taraxacifolia</i> .	Daily for 21 days
10.	AlCl <sub>3</sub> + N-butanol fraction	100 mg/kg body weight of AlCl <sub>3</sub> and 548mg/kg body weight of n-butanol fraction of <i>L. taraxacifolia</i> .	Daily for 21 days
11.	AlCl <sub>3</sub> + Aqueous fraction	100 mg/kg body weight of AlCl <sub>3</sub> and 548mg.kg body weight of aqueous fraction of <i>L. taraxacifolia</i> .	Daily for 21 days

Key: LD = Low dose; MD = Middle dose; HD = High dose

### 2.8 Novel Object Recognition Test (NORT)

Exploration of novelty in an open field has been widely utilized as a measure of behaviour, cognition, memory and brain functions in experimental animals in neuroscience (Ennaceur *et al.*, 2019). The NORT was performed in a wooden open box apparatus measuring 72 x 72 x 36cm. The object to be differentiated were of two different shapes and colours and were heavy enough to prevent displacement by the animal during the test. The task procedure consists of three phases: habituation, familiarization and the test phase. In the habituation phase, each animal was allowed freely exploring the open field arena in the absence of objects for four days. Familiarization and test phases took place in the 5<sup>th</sup> day. During the familiarization phase, a single animal was placed in the open field arena containing two identical sample objects (FO<sub>1</sub>) and (FO<sub>2</sub>) to explore for 5 minutes. FO<sub>1</sub> and FO<sub>2</sub> were

placed in opposite corners of the box. During the test phase, a novel object (NO) was switched with one of the objects (FO<sub>2</sub>) used during familiarization phase and each rat was left in the box to explore for 3 minutes. The time spent exploring the familiar object (FO<sub>1</sub>) and the novel object (NO) was recorded separately, and the discrimination index (DI) was calculated as:

$$DI = \frac{NO - FO_1}{NO + FO_1}$$

The apparatus was cleaned with alcohol and the position of the two objects during the test phase was changed randomly to avoid place preference and the influence of olfactory stimuli.

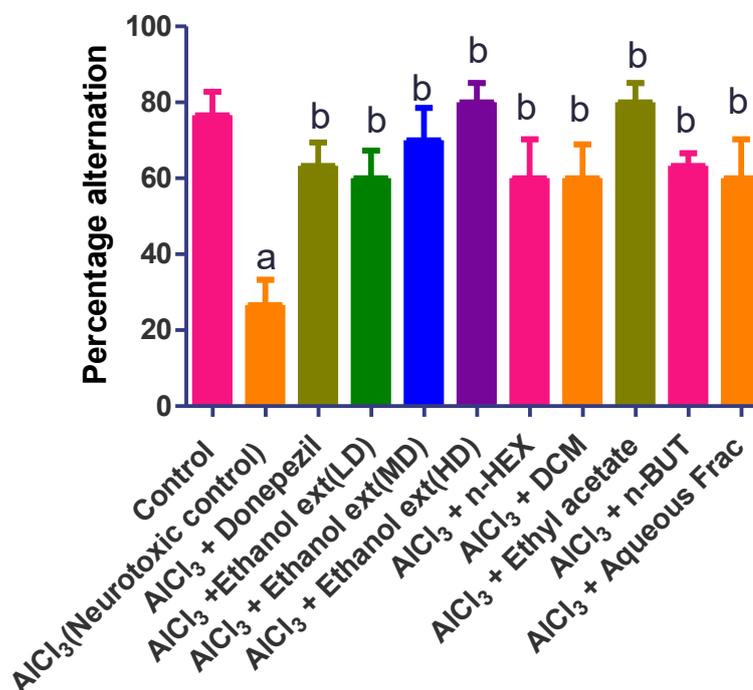
### 2.9 Statistical Analysis

Data were expressed as mean ± standard error of mean (SEM). Differences between mean values were evaluated by analysis of variance (ANOVA), followed by Tukey's post-hoc test for pairwise comparisons. Values of  $p < 0.05$  were considered statistically significant. GraphPad Prism 7.0 software (Graph Pad Inc., USA) was used for the statistical analysis.

## 3. Results

### 3.1 Percentage (%) Alternation of Rats during T-Maze Simple Alternation Test

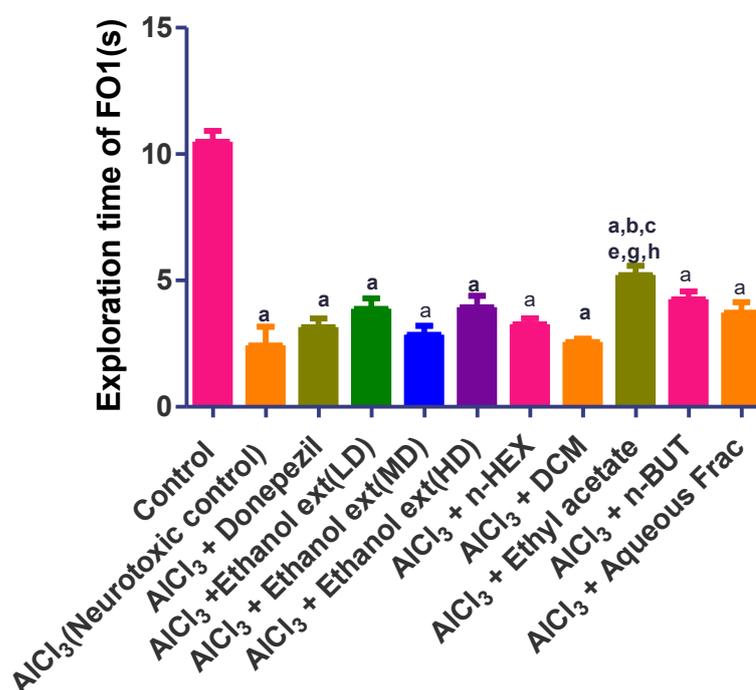
The effect of ethanol extract and fractions of *L.taraxacifolia* on percentage alternation of rats is reported in **Figure 1**. From the result, percentage alternation was significantly ( $p < 0.05$ ) decreased in the AlCl<sub>3</sub> (neurotoxic control) treated group when compared with the control. Percentage alternation was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + donepezil, AlCl<sub>3</sub> + ethanol extract (LD), AlCl<sub>3</sub> + ethanol extract (MD), AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction, AlCl<sub>3</sub> + n-butanol fraction and AlCl<sub>3</sub> + aqueous fraction treated groups when compared with the AlCl<sub>3</sub> (neurotoxic control) respectively.



**Figure 1.** Comparison of percentage (%) alternation of rats during T-maze simple alternation test for control and treatment groups. Columns represent mean ± SEM, n = 6, a =  $p < 0.05$  when compared with the control, b =  $p < 0.05$  when compared with AlCl<sub>3</sub> (neurotoxic control).

### 3.2 Exploration Time of Familiar Object (FO<sub>1</sub>) during Novel Object Recognition Test (NORT)

The effect of ethanol extract and fractions of *L.taraxacifolia* on exploration time of familiar object is reported in **Figure 2**. From the result, exploration time of FO<sub>1</sub> was significantly ( $p < 0.05$ ) decreased in the AlCl<sub>3</sub> (neurotoxic control), AlCl<sub>3</sub> + donepezil, AlCl<sub>3</sub> + ethanol extract (LD), AlCl<sub>3</sub> + ethanol extract (MD), AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction, AlCl<sub>3</sub> + n-butanol fraction and AlCl<sub>3</sub> + aqueous fraction treated groups when compared with the control respectively. Exploration time of FO<sub>1</sub> was significantly increased in the AlCl<sub>3</sub> + ethyl acetate fraction treated group when compared with AlCl<sub>3</sub> (neurotoxic control). Exploration time of FO<sub>1</sub> was significantly increased in the AlCl<sub>3</sub> + ethyl acetate fraction treated group when compared with AlCl<sub>3</sub> + donepezil treated group. Exploration time of FO<sub>1</sub> was significantly increased in the AlCl<sub>3</sub> + ethyl acetate fraction treated group when compared with the AlCl<sub>3</sub> + n-hexane fraction treated group. Exploration time of FO<sub>1</sub> was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + ethyl acetate fraction treated group when compared with the AlCl<sub>3</sub> + DCM fraction treated group.

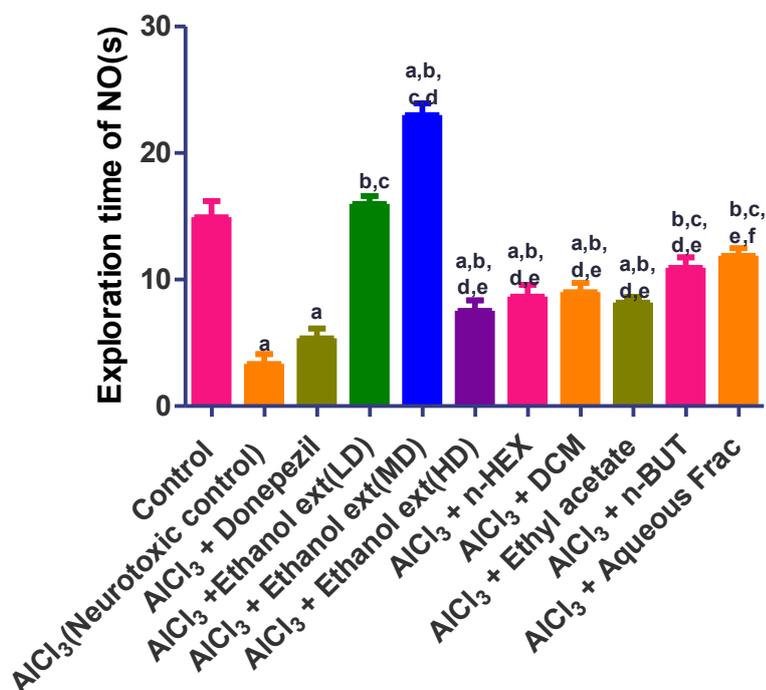


**Figure 2.** Exploration time of familiar object (FO<sub>1</sub>) during novel object recognition test in different experimental groups after 21 days. Columns represent mean  $\pm$  SEM,  $n = 6$ ,  $a = p < 0.05$  when compared with control,  $b = p < 0.05$  when compared with AlCl<sub>3</sub> (neurotoxic control),  $c = p < 0.05$  when compared with AlCl<sub>3</sub> + Ethanol ext (LD),  $e = p < 0.05$  when compared with AlCl<sub>3</sub> + Ethanol ext (MD),  $g = p < 0.05$  when compared with AlCl<sub>3</sub> + N-Hexane,  $h = p < 0.05$  when compared with AlCl<sub>3</sub> + DCM.

### 3.3 Exploration Time of Novel Object (NO) during Novel Object Recognition Test

The effect of ethanol extract and fractions of *L.taraxacifolia* on exploration time of novel object is reported in **Figure 3**. From the result, exploration time of NO was significantly ( $p < 0.05$ ) decreased in the AlCl<sub>3</sub> (neurotoxic control), AlCl<sub>3</sub> + donepezil, AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction treated groups when compared with the control respectively. Exploration time of NO was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + ethanol extract (MD) treated group when compared with the control. Exploration time of NO was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + donepezil, AlCl<sub>3</sub> + ethanol extract (LD), AlCl<sub>3</sub> + ethanol extract (MD), AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction and AlCl<sub>3</sub> + aqueous fraction treated groups when compared with the AlCl<sub>3</sub> (neurotoxic control) respectively. Exploration time of NO was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + ethanol extract (MD), AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl

acetate fraction and AlCl<sub>3</sub> + aqueous fraction treated groups when compared with AlCl<sub>3</sub> + donepezil treated group respectively. Exploration time of NO was significantly ( $p < 0.05$ ) increased in the AlCl<sub>3</sub> + ethanol extract (MD) when compared with AlCl<sub>3</sub> + ethanol extract (LD). Exploration time of NO was significantly ( $p < 0.05$ ) decreased in the AlCl<sub>3</sub> + n-butanol fraction and AlCl<sub>3</sub> + aqueous fraction treated groups when compared with the AlCl<sub>3</sub> + ethanol extract (LD) treated group respectively. Exploration time of NO was significantly ( $p < 0.05$ ) decreased in the AlCl<sub>3</sub> + Ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction, AlCl<sub>3</sub> + n-butanol fraction and AlCl<sub>3</sub> + aqueous fraction when compared with the AlCl<sub>3</sub> + ethanol extract (MD) treated group respectively.



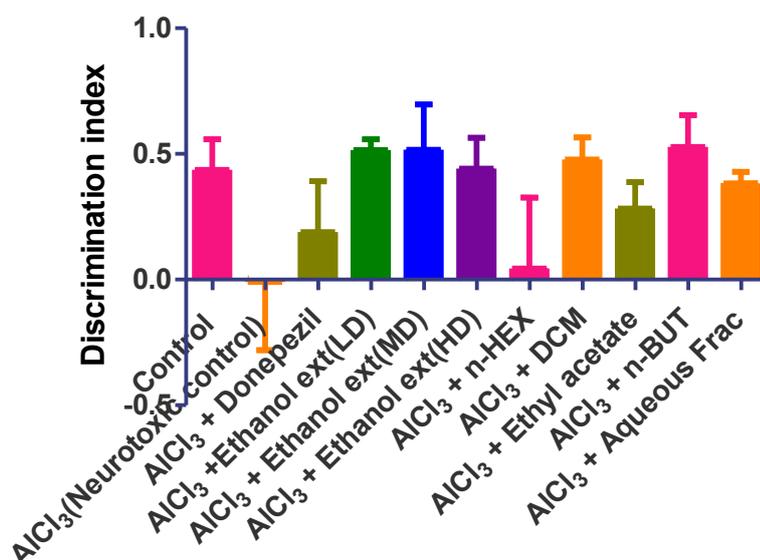
**Figure 3.** Exploration time of novel object (NO) during novel Object recognition test (NORT) in different experimental groups after 21 days. Columns represent mean  $\pm$  SEM,  $n = 6$ ,  $a = p < 0.05$  when compared with control,  $b = p < 0.05$  when compared with AlCl<sub>3</sub> (neurotoxic group),  $c = P < 0.05$  when compared with AlCl<sub>3</sub> + Ethanol ext (LD),  $d = p < 0.05$  when compared with AlCl<sub>3</sub> + Donepezil,  $e = p < 0.05$  when compared with AlCl<sub>3</sub> + Ethanol ext (MD),  $f = p < 0.05$  when compared with AlCl<sub>3</sub> + Ethanol ext (HD).

### 3.4 Discrimination Index (DI) during Novel Object Recognition Test

The effect of ethanol extract and fractions of *L.taraxacifolia* on discrimination index is reported in **Figure 4**. From the result, discrimination index was not significantly different in the AlCl<sub>3</sub> (neurotoxic control), AlCl<sub>3</sub>+ donepezil, AlCl<sub>3</sub>+ ethanol extract (LD), AlCl<sub>3</sub> + ethanol extract (MD), AlCl<sub>3</sub> + ethanol extract (HD), AlCl<sub>3</sub> + n-hexane fraction, AlCl<sub>3</sub> + DCM fraction, AlCl<sub>3</sub> + ethyl acetate fraction, AlCl<sub>3</sub> + n-butanol fraction, AlCl<sub>3</sub> + aqueous fraction treated groups when compared with the control respectively.

## 4. Discussion

The effect of ethanol extract and fractions of *L.taraxacifolia* on percentage alternation of rats was reported in this study. Percentage alternation is a parameter that is used to evaluate cognitive function in rodents. The T-maze simple alternation test is a behavioural assay that evaluates spatial memory and learning in rodents. In the T-maze simple alternation test, the extracts were evaluated for their ability to improve spatial memory and learning in rats. Spontaneous alteration behaviour using the T-maze test has been considered an indicator of memory function in rodents (Hritcu *et al.*, 2011). Here, rats are expected to recall the maze arm that was last visited and try to enter another different arm as possible.



**Figure 4.** Discrimination index (DI) during novel object recognition test in different experimental groups after 21 days. Columns represent mean  $\pm$  SEM, n = 6.

The total amount of arm entries is recorded, and a percentage alternation is calculated. Animal cognition is then assessed based on the score and low scores are considered as cognitively impaired. Furthermore, exposure to aluminium chloride has been reported to alter spontaneous alternation behaviour in rodents (Bourdineaud *et al.*, 2012). In this study, the percentage alternation of rats shows that AlCl<sub>3</sub> (neurotoxic control) treated group displayed a significant decrease in percentage alternation when compared with the control group, indicating impaired cognitive function, thus suggesting that these rats were unable to fully remember which arm they entered last. The decrease could also be accounted for by the tendency of aluminium chloride in generating reactive oxygen species. The massive production of reactive oxygen species could lead to exacerbation and depletion of neuroprotective moieties especially in the hippocampal and prefrontal cortex regions of the brain that are directly involved in memory processes. This resultant effect is memory impairment and cognitive deficit as reflected in the results of this study. The administration of aluminium chloride has been reported in this study to significantly induce oxidative stress presented by significantly increasing MDA while significantly reducing SOD, catalase and glutathione peroxidase. These findings therefore corroborate other scientific reports that suggested aluminium chloride to show a potent neurotoxic property as it promoted the inflammatory process and oxidative stress (Pike *et al.*, 2015). Result from this study also revealed, significant increase in percentage alternation of rats in the donepezil, ethanol extract (low, middle and high doses), n-hexane, DCM, ethyl acetate, n-butanol and aqueous fraction treated groups when compared with the AlCl<sub>3</sub> treated group (neurotoxic control) respectively. This suggests that donepezil, ethanol extract (low, middle and high doses) n-hexane, DCM, ethyl acetate, n-butanol and aqueous fraction protected against cognitive deficit induced by aluminium chloride in the T-maze task. This could be as a result of the memory enhancing effect of the naturally occurring phytochemical constituents of *L.taraxacifolia*. Result from this study also showed that percentage alternation of rats was higher in ethanol extract (high dose) and ethyl acetate treated groups when compared with donepezil treated group respectively. This suggests that the memory enhancing effect exhibited by ethanol extract (high dose) and ethyl acetate fraction was more significant than that of donepezil. This study suggests that the extracts and fractions of *L.taraxacifolia* showed significant improvement in spatial memory and learning in rats. The improved spatial memory and learning may be due to the neuroprotective effects of the extracts and fractions which may be related to their antioxidant and anti-inflammatory properties. Aluminium chloride caused cognitive impairment in rats. Donepezil, a standard neuroprotective drug, improved cognitive function. *L. taraxacifolia* and its fractions exhibited significant neuroprotection by improving cognitive function.

Assessment of memory of rats exposed to AlCl<sub>3</sub> and ethanol extract and fractions of *L.taraxacifolia* by novel object recognition test (NORT) is reported in this study. The test is a cognitive assay that evaluates memory

and exploratory behaviour in rodents. Exploration of novelty in an open field has been widely utilized as a measure of behaviour, cognition, memory and brain functions in experimental animals in neuroscience (Ennaceur *et al.*, 2019). The novel object recognition test measures the natural tendency of a rat to explore a novel object against a familiar object.

Exploration time of familiar object (FO<sub>1</sub>) by novel object recognition test was reported in this study. Result revealed that the exploration time of familiar object in rats in the AlCl<sub>3</sub>, donepezil, ethanol extract (low, middle and high doses), n-hexane, DCM, ethyl acetate, n-butanol and aqueous fraction treated groups was significantly reduced when compared with the control group, respectively. A marked impairment in memory recognition was recorded in the AlCl<sub>3</sub>exposed rats (neurotoxic control) when compared with the control group. The exploration time of familiar object in rats in the ethyl acetate treated group was significantly higher when compared with the AlCl<sub>3</sub>and donepezil treated groups respectively.

Exploration time of novel object (NO) by novel object recognition test was reported in this study. Result revealed that the exploration time of novel object in rats in the AlCl<sub>3</sub> treated group was significantly reduced when compared with the control group. A remarkable impairment in memory recognition and memory deficit was recorded in the AlCl<sub>3</sub> exposed rats (neurotoxic control) when compared with the control group. The exploration time of novel object in rats in the ethanol extract (low, middle and high doses), n-hexane, DCM, ethyl acetate, n-butanol and aqueous fraction treated groups was significantly higher when compared with the AlCl<sub>3</sub> treated group (neurotoxic control) respectively. This suggests that ethanol extract (low, middle and high doses), n-hexane, DCM, ethyl acetate, n-butanol and aqueous fraction significantly improved memory recognition and rescue memory deficit, showing that ethanol extract and fractions of *L.taraxacifolia* protected against aluminium chloride-induced non-spatial memory deficit in the novel object recognition task. Result also revealed that the exploration time of novel object in rats in the ethanol extract (low and middle doses) treated groups was significantly higher when compared with the donepezil treated group. The improved memory recognition may be due to the neuroprotective effect of the extracts and fractions, which may be related to their antioxidant and anti-inflammatory properties. This suggests that the extracts and fractions are more potent than the standard drug(donepezil).

The effect of ethanol extract and fractions of *L. taraxacifolia* on discrimination index was reported in this study. The discrimination index is a parameter used to evaluate the ability of rats to differentiate between a novel object and a familiar object during the novel object recognition test. Findings from this study reveal that rats treated with ethanol extract and its fractions were observed to have spent significantly more time exploring the novel object (NO) than the familiar object (FO) and had a significantly higher discrimination index except n-hexane treated group. This agrees with previous studies demonstrating the potent memory enhancing activity of *phyllanthus amarus* and other plant extracts in experimental models of cognitive impairment (Balmus and Ciobica, 2017; Enogieru and Momodu, 2021). Findings also showed that no significant difference was observed in the exploration time of familiar object and that of novel object in rats treated with aluminium chloride. This contradicts earlier findings reported by Justin-Thenmozhi *et al.*, (2018) that rats treated with aluminium chloride spent more time exploring the familiar object than the novel object.

#### 4. Conclusion

*Launaea taraxacifolia* leaf extract and its fractions (n-hexane, dichloromethane, ethyl acetate, n-butanol and aqueous) exhibited neuroprotective effects against aluminium chloride neurotoxicity in rats, improving cognitive and visuospatial functions. This study demonstrated the neuroprotective potential of ethanol leaf extract and fractions of *L. taraxacifolia* in mitigating aluminium chloride-induced neurotoxicity in rats. Aluminium chloride exposure significantly impaired motor coordination, cognitive flexibility, and visuospatial functions, as observed in reduced hanging time, increased foot slips, prolonged crossing time, decreased percentage alternation in the T-maze, and diminished novel object exploration. However, treatment with *L. taraxacifolia* extracts and fractions significantly improved these parameters, indicating enhanced neuromuscular strength, cognitive processing, and spatial memory. These findings suggest that *L. taraxacifolia* possesses neuroprotective

properties that may counteract neurodegenerative effects associated with aluminium toxicity. Further studies are needed to elucidate the underlying mechanisms and potential clinical applications of this plant in managing neurodegenerative disorders.

### Ethical Issues

This study was done in accordance with international guidelines for care and use of laboratory animals and approval of Faculty of Basic Medical Sciences Research and Ethical Committee (FBMSREC), University of Uyo with the ethical number UU\_FBMSREC\_2024\_002.

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