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Neuroprotective Effects of *Phoenix dactylifera L.* and Melatonin on Aluminum Chloride-induced Neurotoxicity in the Cerebellum of Adult Male Wistar Rats

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ABSTRACT

Exposure to aluminium is associated with neurotoxicity, affecting various parts of the nervous system. The study investigated the neuroprotective potential of ethanolic fruit extract of *Phoenix dactylifera* (EFPD) and melatonin against aluminium chloride ($AlCl_3$)-induced neurotoxicity in male adult Wistar rats. Rats were divided into six groups: group 1 received 0.2 ml distilled water; group 2 received 5 mg/kg $AlCl_3$; group 3 received 10 mg/kg melatonin and 5 mg/kg $AlCl_3$; group 4 received 500 mg/kg EFPD and 5 mg/kg $AlCl_3$; group 5 received 1000 mg/kg EFPD and 5 mg/kg $AlCl_3$; group 6 received 670 mg/kg vitamin E and 5 mg/kg $AlCl_3$. Extracts were administered for two weeks. At the end of the study, the cerebellum was dissected for histopathological analysis, and blood samples were collected for biochemical assays. Sensory-motor and motor coordination were assessed using Foregrip strength and beam walking tests. Results revealed that oral administration of $AlCl_3$ significantly ($p<0.05$) increased lipid peroxidation levels (malondialdehyde) and significantly ($p<0.05$) reduced antioxidant enzyme activities (superoxide dismutase, glutathione peroxidase), leading to neuronal degeneration of Purkinje cells in the cerebellum. However, oral administration of melatonin, EFPD, and vitamin E significantly ($p<0.05$) decreased lipid peroxidation levels and significantly ($p<0.05$) increased antioxidant activities, preserving Purkinje cell cytoarchitecture. These findings suggest that *Phoenix dactylifera* fruit extract and melatonin possess neuroprotective properties against aluminium-induced neurotoxicity, as evidenced by restored antioxidant levels and preserved cerebellar cytoarchitecture. These results highlight the therapeutic potential of natural compounds in mitigating the harmful effects of aluminium toxicity on the central Nervous system.

Keywords: *Phoenix dactylifera*, Vitamin E, Purkinje cells, antioxidant, aluminium chloride

INTRODUCTION

Aluminum (Al) is widespread in our environment, with food serving as the primary source of intake in physiological conditions [1]. The pervasive distribution of aluminium in both environmental settings and food sources poses challenges in avoiding exposure to this metal ion. A connection between aluminium-induced neurotoxicity and excitotoxicity has been established, particularly highlighting aluminium's potential to act as a prooxidant[2]. Interestingly, aluminium has been observed to interact with the superoxide radical, thus augmenting its deleterious effects. Experimental findings underscore the significance of superoxide generation in contributing to excitotoxicity-mediated neuronal demise, primarily through the production of peroxynitrite[3]. Notably, a crucial step in the excitotoxic cascade is the formation of peroxynitrite from superoxide and nitric oxide (NO) during excitotoxicity[4]. In addition, aluminium may exacerbate excitotoxicity by inducing apoptosis in astrocytes, which among neuronal cell populations are considered primary targets for aluminium accumulation among neuronal cells[5]. Furthermore, aluminium has been demonstrated to markedly reduce neuronal levels of reduced glutathione, with astrocytes serving as the principal suppliers of glutathione to neurons[6].

Melatonin, a widespread natural compound resembling neurotransmitters, is synthesized by the pineal gland situated in the brain as a component of the diencephalon[7]. Its multifaceted roles encompass the regulation of circadian rhythms, energy metabolism, and immune functions, alongside its antioxidative properties and involvement in ageing processes[8,9]. While melatonin is generated in various tissues across vertebrates, the majority is synthesized within the pineal gland, subsequently released into the bloodstream to function as a hormone[10]

Oxidative stress is characterized by an imbalance that results in cellular damage and is caused by the body's inability to detoxify reactive oxygen species (ROS). This has a major role in the development of Alzheimer's disease (AD).

AD patients exhibit elevated levels of free radicals due to amyloid-β (Aβ) deposition, mitochondrial dysfunction, and inflammation[11,12]. Particularly, Aβ plaques induce oxidative stress, leading to increased lysosomal production and disruption of lysosomal membrane function, ultimately resulting in cell death[13]. Melatonin, through upregulating α-secretases and downregulating β- and γ-secretases at the transcriptional level, enhances non-amyloidogenic processing and suppresses amyloidogenic processing of β-amyloid precursor protein (βAPP), according to recent research.[14]. Melatonin given over an extended period significantly reduces the cortical mRNA expression of three antioxidant enzymes in human amyloid precursor protein (APP) and presenilin-1 (PS1) transgenic mice, or APP+PS1 double-transgenic animals (SOD-1, glutathione peroxidase, and catalase)[15]. Additionally, Rudnitskaya *et al*. showed that melatonin prevents the decline in mitochondrial volume and improves mitochondrial ultrastructure in hippocampal CA1 neurons of OXYS rats.[16]

Phoenix dactylifera L., commonly known as date palm, is extensively utilized in traditional medicine to address a range of ailments and disorders, including memory disturbances, fever, inflammation, paralysis, and nervous disorders [17,18]. Numerous studies have underscored the nutritional richness of date palm, highlighting its high dietary fibre content and abundance of essential minerals such as phosphorus, iron, potassium, calcium, and vitamins [19,20]. Additionally, research on date palm extracts has revealed their antioxidant properties, attributed to a diverse array of phenolic and flavonoid compounds, as well as certain vitamins present in the fruit [21 - 23].

This study aims to evaluate the neuroprotective effects of melatonin and ethanolic extract from Phoenix dactylifera against aluminium chloride-induced neurotoxicity in the cerebellum of adult Wistar rats. This investigation aims to elucidate potential therapeutic and preventive strategies that may mitigate the deleterious impact of aluminium on cerebellar function.

MATERIALS AND METHODS

Phoenix dactylifera L. (Date Palm)

A mechanical grinder was utilized in the Mile 1 Market in Port Harcourt, Rivers State, Nigeria, to grind the dried fruits of *Phoenix dactylifera* L., also known as date palms.

Experimental animals

The Department of Human Anatomy, Faculty of Medicine, University of Port Harcourt, Rivers State, Nigeria, Animal House provided a cohort of thirty (30) mature male Wistar rats weighing between 90 and 135 g. The rats were kept in wire cages in the Animal House of the Department of Human Anatomy at Rivers State University in Port Harcourt. Before the start of the research, the rats were allowed to acclimate for two weeks. Throughout the study duration, all animals received standard rat pellets (Vital Feeds) and access to water ad libitum. The treatment groups were administered with ethanol fruit extract of Phoenix dactylifera, aluminium chloride, vitamin E, and melatonin, in addition to standard water and rat pellets. All Rats were handled according to the standard guide for the care and use of Laboratory animals. This research was approved by the Faculty of Basic Medical Sciences ethical committee (RSU/FBMSEC/2022/023)

Aluminium chloride: A quantity of 20 grams of aluminium chloride was procured from Joechem stores in Choba, Port Harcourt, and employed as the neurotoxicant in the experiment. This product, manufactured by British Drug Houses (BDH) chemicals in Poole, England, was utilized for the study.

Vitamin E: Used as a reference antioxidant in the experiment, vitamin E was obtained from Iloabuchi, a store located in Port Harcourt. The product used in the trial was produced in Mumbai, India by Livealth Biopharma Private Limited.

Melatonin: Purchased from Barata Pharmacy, 416 Ikwerre Road, Rumuokwuta, Port Harcourt, Rivers State, melatonin was utilized in the experiment as an antioxidant. The manufacturer of the product is Puritan's Pride, INC., located at Holbrook, NY 11741 U.S.A.

Extract preparation

The ethanol fruit extracts of *Phoenix dactylifera* were prepared at the Department of Pharmacology, Faculty of Basic Medical Sciences, Rivers State University, Port Harcourt, Nigeria. The maceration method, as earlier described [21], for ethanol extraction of *Phoenix dactylifera* L. fruit, was followed. The flesh of the dried P. dactylifera L. fruits was manually separated from the pits and ground into a powder using a grinding machine. Subsequently, approximately 250 grams of the powder were soaked in 1 litre of ethanol in a conical flask. After 24 hours, the solution (a mixture of date palm fruit powder and ethanol) was filtered using filter paper and a funnel. The filtrate was left to settle, and the supernatant was decanted. The supernatant was then evaporated to dryness in an evaporating dish using an H-H Digital laboratory Thermostatic Water Bath.

Experimental design

Thirty (30) adult Male Wistar rats were used and divided into six (6) groups of 5 rats in each group as shown in the table below

Table 1: Treatment of experimental animals

Groups	Treatment/day
1	Distilled H_2O (0.2 ml)
2	$AlCl_3$ (5 mg/kg)
3	Melatonin (10 mg/kg) + $AlCl_3$ (5 mg/kg)
4	EFPD (500 mg/kg b.w) + $AlCl_3$ (5 mg/kg)
5	EFPD (1000 mg/kg) + $AlCl_3$ (5 mg/kg)
6	Vit. E (670 mg/kg) + $AlCl_3$ (5 mg/kg)

EFPD= Ethanol Fruit extract of Phoenix dactylifera L, $AlCl_3$= Aluminum chloride, Vit. E= Vitamin E, Route = Oral, Duration = 14 Days

Motor coordination and balance assessments were conducted utilizing the following procedures:

Forelimb Grip Strength Test

This test was performed according to the protocol earlier outlined [19]. Each rat's forepaws were positioned on a horizontally suspended metal wire, measuring 1.05 meters in length and positioned 1 meter above the ground. A basket filled with sawdust served as bedding underneath the wire. With a maximum permitted period of two minutes per rat, the amount of time each rat stayed hanging before slipping off the wire was noted. It's noteworthy that rats were habituated to the setup for two consecutive days before testing (i.e., before treatment). Evaluations were conducted after Day 7 and Day 14. Twenty-four (24) hours after the last administration that is Day 15 animals were euthanized.

Beam Walking Test

Animals were given a task in the beam walking test, which involved them walking across a thin beam to an enclosed safety platform, to assess their motor coordination and balance. A wooden beam of 100 cm in length and 3 cm in width was attached to an elevated platform to produce the beam walking balance apparatus used in this test. The beam was suspended 50 cm above the floor, with one end fastened to a goal box and the other to a thin support that was coupled to a start platform. A box filled with sawdust was positioned at the base to cushion any falls. The animals' beam-walking ability was assessed on a 6-point scale, based on their activity level during the test. Before treatment initiation, rats were acclimated to the beam walking apparatus for three consecutive days. Evaluations were conducted after Day 7 and Day 14. Twenty-four (24) hours after the last administration that is Day 15 animals were euthanized. The beam walking balance was cleaned with methylated spirit after each rat's evaluation.

Estimation of enzymatic antioxidant activity

Superoxide dismutase (SOD) activity was assessed using a rat SOD ELISA Kit, provided by WKEA Med Supplies Corp., China, and manufactured by Fine Test China, according to the manufacturer's guidelines. The procedure was conducted following the method described in reference [27]. Glutathione peroxidase (GPx) activity was determined utilizing a GPx ELISA Kit, also supplied by WKEA Med Supplies Corp., China, and manufactured by Fine Test China, following the manufacturer's protocol. The procedure was based on the method outlined in reference [27]. These activity levels were quantified and expressed as µmol/ml.

Estimation of malondialdehyde levels

The thiobarbituric acid reactive substances (TBARS) assay was used to estimate the amount of malondialdehyde (MDA) in serum. The assay is based on the formation of a coloured complex between thiobarbituric acid (TBA) and MDA, a consequence of lipid peroxidation, which may be measured using spectrophotometry [28]. These activity levels were quantified and expressed as μmol/ml.

Routine histological tissue processing

The H&E staining protocol involves fixing tissue in Bouin's solution, dehydrating in alcohol, clearing with xylene, embedding in paraffin, sectioning, mounting on slides, deparaffinizing, rehydrating, staining with hematoxylin and eosin, followed by dehydration and final mounting, readying the slides for microscopic examination [45].

Analytical statistics

The generated data were shown as mean ± SEM. The Statistical Package for Social Sciences, or SPSS, version 26 was used for the analysis. The data on thirty rats were analyzed using one-way analysis of variance (ANOVA), with a significance threshold of $p < 0.05$ used to evaluate differences between groups. The Duncan Multiple Range Test was used in post hoc analysis to look further into notable group differences. Furthermore, when applicable, paired sample t-tests were used to compare means within groups. Value differences were deemed significant when $p<0.05$

RESULTS

When aluminium chloride was administered orally, the levels of malondialdehyde (MDA) increased significantly ($p<0.05$) in comparison to the control group, and the levels of antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase, decreased significantly ($p<0.05$) in comparison to the control group and vitamin E.

As indicated in Table 2, however, the administration of ethanolic extract of Phoenix dactylifera (EFPD) and melatonin led to a significant ($p<0.05$) increase in the activity level of SOD and GPx when compared to the control and Vitamin E, and a significant ($p<0.05$) decrease in MDA levels when compared to the control group.

Table 2: Serum MDA level and antioxidant enzyme activity of Wistar rats

Groups	**Malondialdehyde (**μmol/ml.)	**Superoxide dismutase (**μmol/ml.)	**Glutathione peroxidase (**μmol/ml.)
Control (0.2 ml of H_20)	0.3940±0.05183	0.4320±0.04790	0.07200±0.009706
$AlCl_3$ (5 mg/kg)	0.6140±0.03295[a]	0.1540±0.02657[a]	0.03660±0.003250[a]
$AlCl_3$ (5 mg/kg)+	0.5820±0.02354[ac]	0.1900±0.01703[ac]	0.05300±0.003592[ac]
Mel (10 mg/kg) $AlCl_3$ (5 mg/kg)+	0.5980±0.05919[abc]	0.1580±0.01655[ac]	0.06660±0.003669[abc]
EFPD (500 mg/kg) $AlCl_3$+ EFPD (1000 mg/kg)	0.5850±0.04444[ac]	0.2000±0.04262[abc]	0.04800±0.006124[abc]
$AlCl_3$ (5 mg/kg)+ VIT.E (6 iu)	0.6125±0.03945[ab]	0.2650±0.03279[ab]	0.06250±0.012861[ab]

n=5; Mean±SEM; One-way Anova and Duncan Multiple range Post hoc test. [a]$p<0.05$ when compared to $AlCl_3$ group. [b]$p<0.05$ when compared to the control group; [c]$p<0.05$ when compared to the group administered $AlCl_3$ and Vit E $AlCl_3$= aluminum chloride, Mel= Melatonin, EFPD= Ethanol Extract of *Phoenix dactylifera* L, Vit. E= Vitamin E

Forelimb Grip Strength Study

The muscular strength of Wistar rats was measured using the forelimb grip strength (FGS) test. The FGS is reflected in the forelimb grip strength time (latency time-to-release grip). When compared to the aluminium chloride and EFPD (1000 mg/kg) treated groups, the EFPD (500 mg/kg), the group treated with melatonin and vitamin E exhibited a noteworthy ($p<0.05$) improvement in FGS, particularly on day 14 (Table 3).

Table 3: Fore-Limb Grip Strength Time of Wistar Rats

Groups	Pre-treatment	7 Days after treatment	14 Days after treatment
Control (0.2 ml of H_20)	94.4±20.961[a]	114±6.000[a]	101±19.000[a]
$AlCl_3$ (5 mg/kg)	92.2±16.488[b]	76±12.079[b]	56.6±15.964[b]
$AlCl_3$ (5 mg/kg)+ Mel (10 mg/kg)	120±0.000[ab]	82.2±23.153[ab]	106.6±9.897[ab]
$AlCl_3$ (5 mg/kg)+ EFPD (500 mg/kg)	97.6±15.105[abc]	81±24.033[abc]	97±23.000[abc]
$AlCl_3$+ EFPD (1000 mg/kg)	114.4±5.600[abc]	37.2±21.041[abc]	28.2±8.399[abc]
$AlCl_3$ (5 mg/kg)+ VIT.E (1.2 iu per rat)	120±0.000[ab]	115.8±2.800[ab]	120±0.000[ab]

n=5; Mean±SEM; One-way ANOVA and Duncan Multiple range Post hoc test. [a]$p<0.05$ when compared to $AlCl_3$ group. [b]$p<0.05$ when compared to the control group. [c]$p<0.05$ when compared to the group administered $AlCl_3$ and Vit E. $AlCl_3$= Aluminum Chloride, Mel= Melatonin, EFPD= Ethanol Extract of *Phoenix dactylifera* L, Vit. E= Vitamin E

Beam Walking Test Study

The Wistar rats' motor coordination and balance were evaluated using the beam walking test. The ability to walk on beams was assessed using a 6-point scoring system called the beam (foot-slips) score. Throughout the trial (pre-treatment through day 14 of treatment), the administration of extract had a significant ($p<0.05$) impact on beam score as compared to the control and aluminium chloride treated groups. The EFPD (1,000 mg/kg) and aluminium chloride treated groups showed a substantial ($p<0.05$) decline in motor coordination and balance between pretreatment and treatment, especially on day 14 of treatment, in comparison to the control group.

On the 14th day of treatment, there was a noteworthy improvement in motor coordination and balance observed in the EFPD (500 mg/kg)- treated group as compared to the group treated with aluminium chloride ($p<0.05$). As demonstrated in Table 4 below, on day 14, the administration of EFPD, specifically at the level of 500 mg/kg of the EFPD-treated group, significantly improved motor coordination and balance compared to the group treated with aluminium chloride.

Table 4: Beam Walking Test of Wistar Rats

Groups	Pre-treatment	7 Days after Treatment	14 Days after Treatment
Control (0.2 ml of H_20)	3±0.632	5±I.00[b]	5.6±0.400[c]
$AlCl_3$ (5 mg/kg)	3±0.775[a]	2.6±0.400[a]	2.2±0.200[a]
$AlCl_3$ (5 mg/kg)+ Mel (10 mg/kg)	3.8±0.917[a]	4.4±0.812[b]	4.8±0.735[b]
$AlCl_3$ (5 mg/kg)+ EFPD (500 mg/kg)	4.8±0.583[a]	4.4±0.678[b]	6±0.000[c]
$AlCl_3$+ EFPD (1000 mg/kg)	3.6±0.678[a]	2.2±0.200[a]	2±0.000[a]
$AlCl_3$ (5 mg/kg)+ VIT.E (6 iu)	3.6±0.980[a]	4±0.894[b]	4.2±0.663[b]

n=5; Mean±SEM; AlCl3= Aluminum Chloride, Mel= Melatonin, EFPD= Ethanol Extract of *Phoenix Dactylifera* L, Vit. E= Vitamin E. [a,b] denotes the level of significance a when compared to the control group; b when compared to the aluminium-treated group only.

Histological studies

Histological examination of the cerebellar sections from the control group showed a well-preserved and intact cerebellar cortex with normal morphology of the Purkinje and granule cells and a typical laminar organization of the molecular layer, Purkinje, and granular layers, all of which are indicative of physiological integrity as shown in Figure 1(A).

Photomicrographs of the cerebellum of aluminium-treated rats showed less cellular molecular layer with peri-cellular spaces; the Purkinje cell layer and granular layer were distorted and disorganized (Figure 1B). Aluminium-treated rats that received melatonin displayed restoration of cells in all three layers: the molecular layer showed recovered stellate and basket cells; the Purkinje cell layer showed reorganized and restored Purkinje cells and the granular layer showed some rosette granular cells (Figure 1C). Photomicrograph of cerebellum of rats treated with $AlCl_3$ and low dose *P. dactylifera* section showed organized cytoarchitecture of the molecular layer; Purkinje cell layer and granular layer, normal Purkinje cells, stellate cells and rosette granule cells of the 3 layers of the cerebellar cortex (Figure 1D). The cerebellum of Wistar rats treated with $AlCl_3$ and a high dose of *P. dactylifera* L. showed a molecular layer, mildly distorted Purkinje cell layer, fewer Purkinje cells and reduced granular cells (Figure 1E). The group treated with $AlCl_3$ and Vitamin E showed organized cytoarchitecture of the cerebellar cortical layers, normal Purkinje cells, stellate cells and rosette granule cells of the 3 layers of the cerebellar cortex (Figure 1F).

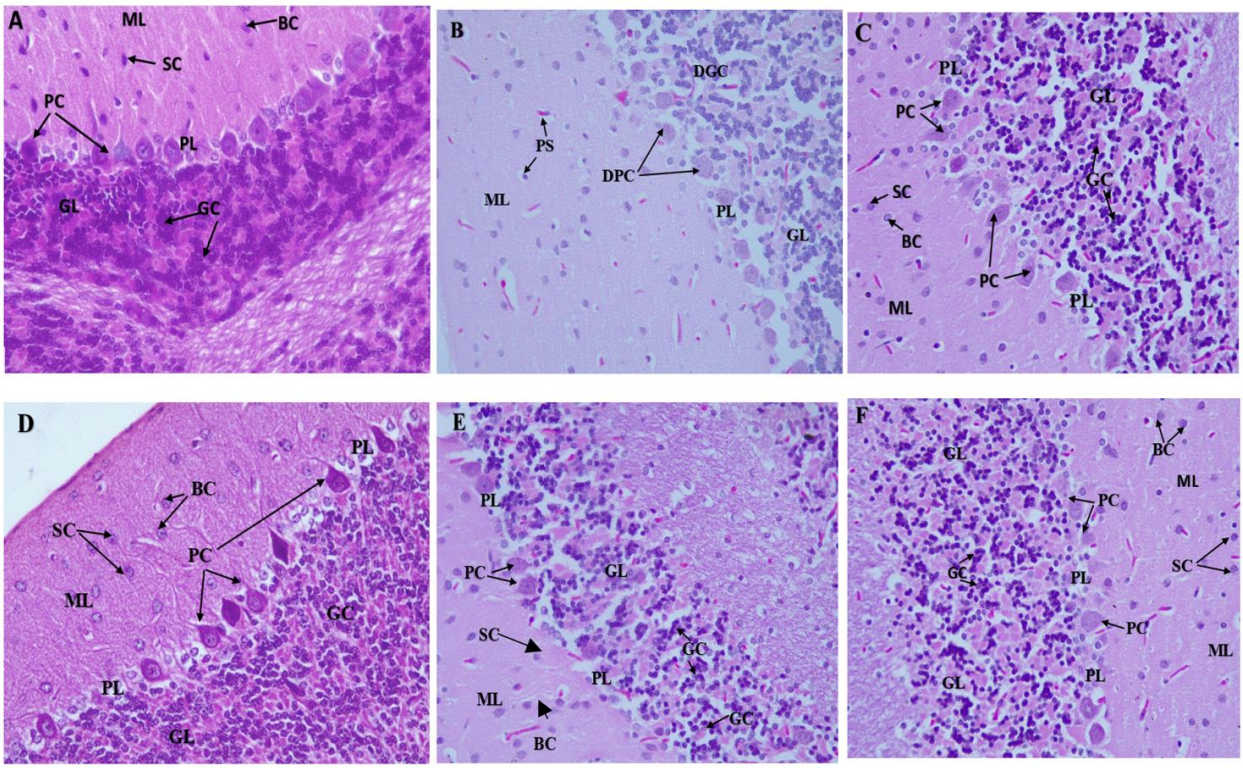

Figure 1(A-D): Photomicrographs of the cerebellar cortex of adult male Wistar rats (A- Control, 0.2 ml distilled water; B- 5 mg/kg $AlCl_3$; C- $AlCl_3$ +10 mg/kg Melatonin; D- $AlCl_3$ + 500 mg/kg *P. dactylifera*; E- $AlCl_3$ 1000 mg/kg *P. dactylifera*; F- $AlCl_3$ and Vit E). H&E x400. BC: basket cell, GC: granule cell, SC: stellate cell, NPC- normal Purkinje cells.

DISCUSSION

The association between aluminium compounds and oxidative stress, leading to neuronal loss, has provided valuable insights into neurodegenerative diseases, given the heightened susceptibility of neurons to free radical damage[30]. Aluminium exposure has been shown to upregulate the expression of numerous genes crucial for cellular growth and function. Oxidative stress also induces DNA damage, a pivotal driver of tissue damage and this is connected to the etiology of a wide range of illnesses and linked with neuronal cell degeneration[31].

The present result revealed that oral administration of $Alcl_3$ reduced the activity level of antioxidant enzymes such as GPx and SOD and increase in level of lipid peroxidation (MDA) as reported by[27].

While promoting the conversion of lipid hydroperoxides (ROOH) and hydrogen peroxide (H_2O_2) into water (H_2O) and the respective alcohols, SOD catalyzes the dismutation of the superoxide radical (O^{2-}) into molecular oxygen (O_2) and hydrogen peroxide (H_2O_2). Collectively both enzymes are known to protect tissues from damage as a result of the generation of free radicals[33].

Data obtained from this study revealed that oral administration of *Phoenix dactylifera* and melatonin resulted in a reduction in levels of MDA and an increase in the activity levels of SOD and GPx [34]

The generation of free radicals can result in a reduction in foregrip strength time in rats by damage to muscle cells resulting from DNA, proteins, and lipid oxidation. For instance, lipid peroxidation can damage cell membrane integrity and compromise muscle fibre performance. Muscle contraction and force production may be impacted by structural changes in contractile proteins brought on by protein oxidation. Muscle cells' energy-producing mitochondria may be targeted by reactive oxygen species (ROS) produced during oxidative stress[35]. Muscle contractility can be hampered and ATP generation compromised by mitochondrial malfunction. Furthermore, damage to mitochondrial DNA brought on by ROS can impair mitochondrial function and intensify oxidative stress hence these can result in a reduction in foregrip strength as a result of damage to muscle integrity[35,36,37]. Free radicals-mediated muscle damage as stated above can also result in altered neuromuscular function, muscle weakness and as a result impaired muscle coordination which resulted in poor performance during the beam walking test in animals administered aluminium chloride only[38]

Oxidative stress can exacerbate excitotoxicity, a process involving excessive activation of glutamate receptors, such as N-methyl-D-aspartate (NMDA) receptors, leading to calcium overload and neuronal damage. Excitotoxicity in the cerebellum can result in neuronal death and dysfunction, impairing motor coordination and balance. This study revealed cerebellar neuronal damage among the group administered $Alcl_3$ as seen in Figure 1B and this result is in agreement with the study carried out by[27] however administration of *Phoenix dactylifera* and Melatonin resulted in the Preservation of Cerebellar architecture which was also reported by[21,41].

Vitamin E mitigates the harmful effects of aluminium on the central nervous system via different mechanisms. As a potent antioxidant, Vitamin E reduces oxidative damage in neuronal cells by scavenging reactive oxygen species (ROS) generated by $AlCl_3$, decreasing lipid peroxidation, and enhancing antioxidant enzyme activities[42]. Vitamin E preserves neuronal integrity and function, ameliorates $AlCl_3$-induced cognitive deficits, prevents neuronal apoptosis and enhances synaptic plasticity, thereby protecting against memory impairments[43]. Through its anti-inflammatory properties, it inhibits pro-inflammatory cytokine production and reduces microglial activation, thereby protecting neurons from neuroinflammation caused by chronic $AlCl_3$ exposure [44].

Our findings revealed that vitamin E enhanced antioxidant activity and neuronal integrity against the deleterious effects of aluminium chloride, and improved forearm grip strength and motor coordination.

Purkinje cells are an essential part of the cerebellum and are involved in motor movement coordination. They receive input from the inferior olive in the brainstem, which is the source of the climbing fibres, and the granule cells in the cerebellar cortex, which is the source of the parallel fibres. Purkinje cells can integrate information about motor commands, motor coordination, and sensory feedback thanks to these inputs. Motor impairment can result from multiple mechanisms when Purkinje cells are lost or injured such as loss of inhibition, loss of feedback control and loss of motor learning [39,40].

CONCLUSION

The study underscores the possible therapeutic effects of melatonin and *Phoenix dactylifera* in lowering oxidative damage and maintaining cerebellar function during aluminium-induced neurotoxicity.

Declaration

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