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Original Paper

MO11 AND MS06 AMELIORATED CADMIUM CHLORIDE-INDUCED NEURO-DEGENERATION AND ALTERATIONS OF DOPAMINE, GLUTAMATE AND MYELIN BASIC PROTEIN EXPRESSIONS IN RATS

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Abstract

This study evaluated the neuro-protective potentials of MO11 (isolated from Moringa oleifera leaves) and MS06 (isolated from Musa sapientum suckers) in Cadmium Chloride ($CdCl_2$)-induced neurotoxicity in rat cerebrum. Twenty-eight adult male wistar rats were randomly divided into 7 groups (n= 4). Group 1 received physiological saline. Groups 2-4 and 7 received single 1.5 mg/Kg bodyweight of $CdCl_2$ (i.p.) (Day 1). Groups 3, 4 and 7 were post-treated with 15 mg/Kg bodyweight of MO11, 15 mg/Kg bodyweight of MO11 + 7 mg/Kg bodyweight of MS06 and 3.35 mg/Kg bodyweight of Doxorubicin respectively (Days 1-17). Groups 5 and 6 received only MO11 and Olive Oil (vehicle) respectively (Days 1-17). Tissue-immunochemical assays of Dopamine, Glutamate and Myelin Basic Protein (MBP) (ELISA technique) and Total Protein assays (spectrophotometric technique) in cerebral homogenates of rats were conducted. Statistical analyses showed upregulations of Dopamine and Glutamate in Groups 3, 4 and 7 compared with Group 2. Furthermore, results showed significant MBP-downregulations in Groups 3 and 4, but non-significant MBP-downregulation in Group 7, compared with Group 2. Total Protein levels were normal in Groups 1-7. MO11 and MS06 provided better neuro-protective and re-myelination potentials compared with Doxorubicin. Overall, MO11 and MS06 possess neuro-protective, neuro-regenerative and re-myelination potentials.

Keywords: *cadmium, Moringa oleifera, Musa sapientum, neuro-protection, neuro-regeneration, neuro-toxicity*

Introduction

Cadmium (Cd) is one of the 10 chemicals of concern for human health [*Andjelkovic et al., 2019; Akinlolu et al., 2022*]. Human Cd-exposure was linked with nervous system dysfunctions resulting in symptoms such as impaired learning capacity, headache and vertigo, decreased cognitive functions, olfactory dysfunction, poor vasomotor functioning, parkinsonian-like symptoms, peripheral neuropathy and poor equilibrium and balance co-ordination. Cd-exposure is equally an etiological

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factor in the development of neuro-degenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD). Increased concentrations in total Cd-exposure was associated with dyslexia or learning difficulties, decreased visual motor capacity and mental retardation in children. Cd-induced neuro-toxicity results from increased oxidative stress, and associated neuronal cell death are cell-specific, with cerebral cortical neurons as main targets [*Batool et al., 2019*]. This makes it relevant that drug compounds from plants or other sources be searched for to ameliorate or prevent Cd-induced neuro-toxicity and neuro-degeneration.

Moringa oleifera (MO) and *Musa sapientum* (MS) are ethno-medicinal plants which are well grown in Nigeria (Akinlolu *et al*., 2021). In addition, MOF6, which was fractionated from MO leaves using column chromatography methods showed significant antioxidant and neuro-protective potentials [*Omotoso et al., 2018; Akinlolu et al., 2020a*], hepato-protective, anti-drug resistance and anti-proliferation potentials [*Akinlolu et al., 2021*] in rats. Furthermore, MSF1, which was fractionated from MS sucker using column chromatography methods possesses hepato-protective, anti-proliferation and anti-drug resistance potentials in 7,12-Dimethylbenz[a]anthracene-induced hepatotoxicity in rats [*Akinlolu et al., 2021*].

The mechanism underlying Cd-induced neurotoxicity remains poorly understood till date. Cd generally exists as a divalent cation, complexed with other elements, such as Cadmium Chloride ($CdCl_2$) [*Andjelkovic et al., 2019*]. In this study, the most active antioxidant and antimicrobial cyto-toxic compounds were isolated from MO leaves (MO11) and MS suckers (MS06) respectively. Therefore, in-order to further understand the mechanisms underlying Cd-induced neuro-toxicity and in-order to determine the neuro-protective and neuro-regenerative potentials of MO and MS, this study examined the effects of MO11 and MS06 on $CdCl_2$-induced neuro-toxicity, neuro-degeneration and de-myelination in the cerebral cortices of adult male wistar rats.

Materials and methods

Ethical Approval; Ethical approval via UERC/ASN/2018/1161 was obtained from the Ethical Review Committee of the University of Ilorin, Nigeria. Appropriate measures were observed to ensure minimal pain or discomfort of rats used in this study. Furthermore, this study was carried out in compliance with internationally accepted principles for laboratory animal use and care as contained in the European Community guidelines (EEC Directive of 1986; 86/609/EEC), the Directive 2010/63/Eu of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes and the Guidelines of the U.S. Public Health Service and NIH regarding the care and use of animals for experimentation (NIH publication #85-23, revised in 985).

Collection, authentication and deposition of MO leaves and MS suckers; MO leaves and MS suckers were obtained locally and freshly from forest reserves in Ilorin, Kwara State, Nigeria. The obtained plant samples were authenticated, deposited, and assigned Herbarium Identification Numbers UILH/001/1249 and UILH/002/1182, respectively, at the herbarium of the Department of Botany, University of Ilorin, Nigeria.

Evaluations of antioxidant and anti-microbial activities of MO and MS fractions; The antioxidant activities of the plant extracts were evaluated using the modified 2,2- diphenyl-1-picrylhydrazyl method as previously described by Chaves *et al*. (2020). In addition, the anti-microbial activities of the plant extracts were evaluated by testing the cytotoxic potential of each fraction against E. coli and Salmonella typhimurium, as previously described by Elisha *et al*. (2017).

Extraction, partitioning of fractions and isolations of MO11 from MO leaves and MS06 from MS suckers; MO11 and MS06 were isolated from *Moringa oleifera* leaves and *Musa sapientum* suckers, respectively, following a series of antioxidant analyses (2,2-diphenyl-1-picrylhydrazyl method), anti-microbial analyses (anti-Escherichia-coli and anti-Salmonella-tiphimurium tests), chromatography, and spectroscopic fractionation techniques, as described previously [Ameen and Akinlolu, 2023].

Chemicals and Reagents; Cadmium Chloride ($CdCl_2$) (Sigma-Aldrich, Tokyo, Japan), Sucrose crystal (Qualikems), Methylated spirit (Samstella Industry Nigeria Limited) were purchased from Bristol Scientific Company, Lagos State, Nigeria and local suppliers respectively. Normal Saline, Doxorubicin and Olive Oil were purchased from Olabisi Onabanjo University Teaching Hospital

pharmacy, Sagamu, Ogun State, Nigeria.

Animal Care and Feeding; Twenty-eight (28) adult male Wistar rats (average weight of 155 *g* and 2 months of age) were purchased from a colony breed at Badagry in Lagos state, Nigeria. The rats were randomly divided into 7 groups with 4 rats per group. The rats were acclimatized for a week at the animal house of the Faculty of Pharmacy of Olabisi Onabanjo University, Sagamu campus, Ogun State, Nigeria before the beginning of experimental procedures. The rats were kept under standard conditions and allowed free access to food and drinking water ad libitum. The experimental procedure lasted for 18 Days. The bodyweights of the rats were measured and recorded on daily bases using electronic compact scale (SF-400C weighs in gram) weighing scale; a product of Valid Enterprise, Kalbadevi, Mumbai, India.

Grouping of Rats and Extracts/Drugs Administration; MO11 and MS06 were dissolved in Olive Oil (vehicle). Rats of Control Group 1 (Baseline Control) received physiological saline only for 17 Days (Days 1 – 17). Each rat of Experimental Groups 2 – 4 and 7 received single intra-peritoneal administration of 1.5 *mg/Kg* bodyweight $CdCl_2$ on Day 1. Rats of Group 2 (Negative Control) were left untreated throughout experimental procedure for 17 Days (Days 1 – 17). Thereafter, rats of Group 3 were post-treated orally with 15 *mg/Kg* bodyweight of MO11 for 17 Days (Days 1 – 17). Rats of Group 4 were post-treated orally with combined mixture of 15 *mg/Kg* bodyweight of MO11 and 7 *mg/Kg* bodyweight of MS06 for 17 Days (Days 1 – 17). Rats of Group 5 received only 15 *mg/Kg* bodyweight of MO11 orally for 17 Days (Days 1 – 17). Rats of Group 6 received only 1 *ml/Kg* bodyweight of Olive Oil (vehicle) orally for 17 Days (Days 1 – 17). Rats of Group 7 were post-treated with intravenous tail administration of 3.35 *mg/Kg* bodyweight of Doxorubicin (standard anticancer drug – Positive Control) for 17 Days (Days 1 – 17).

Completion of experimental procedures; Twenty-four hours after the last day of administration of drugs and extracts on Day 17, the experimental procedures were completed following rats' sacrifice on Day 18 by cervical dislocation.

Evaluations of concentrations of Dopamine, Glutamate and Myelin Basic Protein in homogenates of cerebral hemispheres of rats using Enzyme Linked Immunosorbent Assay (ELISA)

One cerebral hemisphere from each rat was excised and homogenized with the aid of pestle and porcelain mortar in in the proportion of 1 *g* to 4 *ml* of ice-cold sucrose solution (0.25 *M*). The obtained homogenates of cerebral cortices were topped up to 5 *ml* with 0.25 *M* ice-cold sucrose, and transferred into a 5 *ml* serum bottle. Homogenates were later centrifuged for 15 minutes using a centrifuge (Model 90-1) at 3000 revolution per minute. The resultant supernatant was stored at -20 ^{O}C, and evaluated for the cerebral cortices amount of Dopamine, Glutamate and Myelin Basic Protein in all groups of rats by employing ELISA method as previously described by [*Ameen and Akinlolu, 2023*].

Evaluations of Total Protein levels: Total Protein concentrations in the cerebral cortices of all rats of Groups 1 - 7 were evaluated following the protocol contained in Total Protein kit, Micro Lowry (Sigmal-Aldrich TP0300 and L3540). The Total Protein kit, Micro Lowry (Sigmal-Aldrich TP0300 and L3540) employs the modified method of Lowry which is based on Biuret reaction followed by reduction of Folin and Ciocalteu's phenol reagent yielding a purple colour. The absorbance of the coloured solution was then read between 500*nm* – 800*nm*, and Total Protein concentration determined from a calibration curve.

Statistical Analyses: Statistical analyses were conducted using the 2019 Statistical Package for the Social Science software Version 23.0. Computed data of concentrations of each of Dopamine, Glutamate, Myelin Basic Protein and Total Protein were expressed as arithmetic means ± standard error of mean, and were subjected to statistical analyses using One-way Analysis of Variance to test for significant difference amongst Groups 1 – 7. Degree of freedom (df): (between groups and within groups) and F-values were computed. Significant difference was confirmed at 95% confidence interval with associated p-value of less than 0.05 ($p \leq 0.05$). In addition, Scheffe Post-hoc analysis was used for separation of Mean values amongst Groups 1 – 7. The statistical comparison of the concentration of each of Dopamine, Glutamate, Myelin Basic Protein and Total Protein between two groups was considered significant only at $p \leq 0.05$.

Results

Concentrations of Dopamine in cerebral cortices of rats: Results showed statistically significant lower levels of Dopamine ($p \leq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with Normal saline-treated Control Group 1 (df = 6,15, F = 7.30, p = 0.01) as presented in Table 1. In addition, results showed statistically non-significant lower levels of Dopamine ($p \geq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with $CdCl_2$-exposure + MO11 post-treated Group 3 (df = 6,15, F = 7.30, p = 0.15), $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 (df = 6,15, F = 7.30, p = 0.06), MO11-only treated Group 5 (df = 6,15, F = 7.30, p = 0.07), Olive Oil-only treated Group 6 (df = 6,15, F = 7.30, p = 0.24) and $CdCl_2$-exposure + Doxorubicin post-treated Group 7 (df = 6,15, F = 7.30, p = 0.57) as presented in Table 1.

Concentrations of Glutamate in cerebral cortices of rats: Results showed statistically non-significant lower levels of Glutamate ($p \geq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with Normal saline-treated Control Group 1 (df = 6,14, F = 6.66, p = 0.30), $CdCl_2$-exposure + MO11 post-treated Group 3 (df = 6,14, F = 6.66, p = 0.32), $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 (df = 6,14, F = 6.66, p = 0.62), Olive Oil-only treated Group 6 (df = 6,14, F = 6.66, p = 0.13) and $CdCl_2$-exposure + Doxorubicin post-treated Group 7 (df = 6,14, F = 6.66, p = 1.00) as presented in Table 1. In addition, results showed statistically significant lower levels of Glutamate ($p \leq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with MO11-only treated Group 5 (df = 6,14, F = 6.66, p = 0.01) as presented in Table 1.

Results of One-way ANOVA from Days 1 – 17. Mean ± SEM across the columns between groups are significantly different with a>ab>b>c>d>e. (n = 4 per group).

Concentrations of Myelin Basic Protein in cerebral cortices of rats: Results showed statistically significant higher levels of Myelin Basic Protein ($p \leq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with Normal saline-treated Control Group 1 (df = 6,18, F = 65.20, p<0.001), $CdCl_2$-exposure + MO11 post-treated Group 3 (df = 6,18, F = 65.20, p<0.001), $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 (df = 6,18, F = 65.20, p<0.001), MO11-only treated Group 5 (df = 6,18, F = 65.20, p<0.001) and Olive Oil-only treated Group 6 (df = 6,18, F = 65.20, p<0.001) as presented in Table 2. In addition, results showed statistically non-significant higher levels of Myelin Basic Protein ($p \geq 0.05$) in rats of $CdCl_2$-only treated Group 2, when compared with $CdCl_2$-exposure + Doxorubicin post-treated Group 7 (df = 6,18, F = 65.20, p = 0.46) as presented in Table 2.

Concentrations of Total Protein in cerebral cortices of rats: Results showed similar mean levels of Total Protein in rats of $CdCl_2$-only treated Group 2, when compared with Normal saline-treated Control Group 1 (df = 6,18, F = 0.80, p = 1.00), $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 (df = 6,18, F = 0.80, p = 1.00) and Olive Oil-only treated Group 6 (df = 6,18, F = 0.80, p = 1.00) as presented in Table 2. In addition, results show levels of Total Protein ($p \geq 0.05$) in rats of $CdCl_2$- ed statistically non-significant lower only treated Group 2, when compared with $CdCl_2$-exposure + MO11 post-treated

Table 1.

Concentrations of Dopamine, Glutamate, Myelin Basic Protein and Total Protein in cerebral cortices of rats.

	Drug/Extract Administered	Dopamine (*ng/mL*)	P-value*	Glutamate (*pg/mL*)	P-value*
Group 1	Normal Saline only	27.51 ± 2.19^{a}	0.01	132.28 ± 23.25^{b}	0.30
Group 2	$CdCl_2$ only	18.39 ± 3.11^{e}		83.17 ± 4.18^{d}	
Group 3	$CdCl_2$-exposure + MO11 post-treated	24.22 ± 1.22^{b}	0.15	131.43 ± 3.82^{b}	0.32
Group 4	$CdCl_2$-exposure + MO11 + MS06 post-treated	27.29 ± 1.29^{a}	0.06	119.78 ± 20.62^{c}	0.62
Group 5	MO11 only	25.14 ± 0.88^{ab}	0.07	186.28 ± 42.76^{a}	0.01
Group 6	Olive Oil only	23.63 ± 2.03^{c}	0.24	146.54 ± 19.22^{ab}	0.13
Group 7	$CdCl_2$-exposure + Doxorubicin post-treated	22.06 ± 2.43^{d}	0.57	85.72 ± 3.34^{d}	1.00

Notes: *p≤0.05: Group 2 versus Groups 1 and 3 – 7*

Group 3 (df = 6,18, F = 0.80, p = 1.00), MO11-only treated Group 5 (df = 6,18, F = 0.80, p = 0.86) and $CdCl_2$-exposure + Doxorubicin post-treated Group 7 (df = 6,18, F = 0.80, p = 1.00) as presented in Table 2.

Results of One-way ANOVA from Days 1 – 17. Mean ± SEM across the columns between groups are significantly different with a>ab>b>c>d>e. (n = 4 per group).

Discussion

We previously reported that $CdCl_2$-induced neurotoxicity resulted in increased number of chromatolytic cells and neurodegeneration in the prefrontal cortices of rats of $CdCl_2$-only treated Group 2 [*Akinlolu et al., 2022*]. However, post-treatments of $CdCl_2$-induced neurotoxicity with MO11, MO11 + MS06, and Doxorubicin resulted in decreased number of chromatolytic cells in the prefrontal cortices of rats. Hence, MO11, MS06 and Doxorubicin possess neuro-protective potentials and were able to gradually reverse $CdCl_2$-induced chromatolysis and neurodegeneration within 17 days [*Akinlolu et al., 2022*].

Dopamine functions as an inhibitory transmitter and as a stabilizer of brain regions. Dys-regulation of dopaminergic neurons in brain regions such as substantia nigra results in non-stop release of output of excitatory signals of the corticospinal motor control system, and exceeding excitation of body muscles with accompanying rigidity [*Hugo et al., 2016*]. Therefore, Dopamine is involved in the regulations of arousal, motor control, motivation, reinforcement, reward, sexual gratification, nausea and lactation [*Hugo et al., 2016*].

Will $CdCl_2$-exposure alter Dopamine levels in the brain? Results of this study showed significant downregulation of Dopamine in cerebral homogenates of $CdCl_2$l-only treated Group 2, when compared with Normal saline-only treated Control Group 1 (Table 1). This observation indicates that $CdCl_2$-exposure resulted in decreased Dopamine levels, neurotoxicity and neuro-degeneration. The results of this study are in agreement with previous studies which reported Cadmium-induction of decreased Dopamine levels [*El-Tarras et al., 2016; Gupta et al., 2018*] with accompanied motor dysfunctions [*Gupta et al., 2018*], low energy, lack of motivation and depression [*El-Tarras et al., 2016*].

Can MO11, MS06 and Doxorubicin protect the cerebrum against $CdCl_2$-induction of decreased Dopamine levels? Post-treatments of $CdCl_2$-induced neurotoxicity resulted in increased Dopamine levels in cerebral cortices homogenates of rats of $CdCl_2$-exposure + MO11 post-treated Group 3, $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 and $CdCl_2$-exposure + Doxorubicin post-treated Group 7, when compared with $CdCl_2$-only treated Group 2 as presented in Table 1. These observations indicate that MO11, MS06 and Doxorubicin possess neuro-protective and neuro-regenerative potentials.

Glutamate is the most abundant free amino acids and the major excitatory neurotransmitter in the brain. Glutamate is at the cross-road of several metabolic pathwyas and could cause excito-toxicity when excessively excited. Hence, too little or

Table 2.

Concentrations of Myelin Basic Protein and Total Protein in cerebral cortices of rats.

Drug/Extract Administered	Myelin Basic Protein (*pg/mL*)	P-value*	Total Protein (*mg/dL*)	P-value*
Group 1 Normal Saline only	1.16±0.01^{b}	p<0.001	8.77±0.33^{c}	1.00
Group 2 $CdCl_2$ only	2.18±0.07^{a}		8.88±0.14^{c}	
Group 3 $CdCl_2$-exposure + MO11 post-treated	1.13±0.01^{b}	p<0.001	9.43±0.88^{b}	1.00
Group 4 $CdCl_2$-exposure + MO11 + MS06 post-treated	1.10±0.02^{b}	p<0.001	8.86±0.37^{c}	1.00
Group 5 MO11 only	1.07±0.06^{c}	p<0.001	26.16±35.16^{a}	0.86
Group 6 Olive Oil only	1.07±0.02^{c}	p<0.001	8.47±0.60^{c}	1.00
Group 7 $CdCl_2$-exposure + Doxorubicin post-treated	1.97±0.30^{ab}	0.46	13.63±1.80^{ab}	1.00

Notes: *p≤0.05: Group 2 versus Groups 1 and 3 – 7*

too much Glutamate is harmful to the body system requiring cells to have the right glutamate-sensitivity, withstand normal glutamate-stimulation and remove Glutamate at normal rates from the right places (Pal, 2021).

Will $CdCl_2$-exposure alter Glutamate levels in the brain? Results of this study showed decreased Glutamate levels in cerebral homogenates of $CdCl_2$-only treated Group 2, when compared with Normal saline-only treated Control Group 1 (Table 1). This observation indicates that $CdCl_2$-exposure resulted in decreased Glutamate levels and induction of neurotoxicity. In addition, Glutathione which is derived from Glutamate, Cysteine and Glycine, is the major redox buffer in the cell, and the first line of defense against oxidative stress [*Branca et al., 2020*]. The observed $CdCl_2$-induction of decreased Glutamate levels in this study imply that $CdCl_2$-induced neurotoxicity could result in increased oxidative stress. Furthermore, the results of this study are in agreement with previous studies which reported Cadmium-induction of decreased Glutamate levels in the hypothalamus of rats, and reported Cadmium-induction of oxidative stress [*Elkhadragy et al., 2018*].

Can MO11, MS06 and Doxorubicin protect the cerebrum against $CdCl_2$-induction of decreased Glutamate levels? Post-treatments of $CdCl_2$-induced neurotoxicity resulted in increased Glutamate levels in cerebral cortices homogenates of rats of $CdCl_2$-exposure + MO11 post-treated Group 3, $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4 and $CdCl_2$-exposure + Doxorubicin post-treated Group 7, when compared with $CdCl_2$-only treated Group 2 as presented in Table 1. These observations indicate that MO11, MS06 and Doxorubicin possess neuro-protective and neuro-regenerative potentials.

Myelin Basic Protein (MBP) is the next abundant myelin protein second to proteolipid protein. It functions as an actin-binding membrane protein and is involved in transmitting extracellular signals to tight junctions of myelin and to the cytoskeleton of oligodendrocytes (Afifi and Embaby, 2016). Astrocytes' depletion result in breach of the glial-limiting membrane, Schwann cells' invasion for myelin sheath repair and MBP's dissociation from the plasma membrane. Loss of myelin sheath (de-myelination) results from response to axonal degeneration and consequent oxidative stress [*Afifi and Embaby, 2016*]. Therefore, MBP-upregulation is associated with demyelination [*Akinlolu et al., 2020b*].

Will $CdCl_2$-exposure alter MBP levels in the brain? Results of this study showed significant increased MBP levels in cerebral homogenates of $CdCl_2$-only treated Group 2, when compared with Normal saline-only treated Control Group 1 (Table 2). This observation indicates that $CdCl_2$-exposure resulted in increased MBP levels, neurotoxicity and induction of demyelination.

Can MO11, MS06 and Doxorubicin protect the cerebrum against $CdCl_2$-induction of increased MBP levels? Post-treatments of $CdCl_2$-induced neurotoxicity resulted in significant decreased MBP levels in cerebral cortices homogenates of rats of $CdCl_2$-exposure + MO11 post-treated Group 3 and $CdCl_2$-exposure + MO11 + MS06 post-treated Group 4, when compared with $CdCl_2$-only treated Group 2 as presented in Table 2. These observations indicate that MO11 and MS06 possess significant re-myelination, neuro-protective and neuro-regenerative potentials.

However, post-treatments of $CdCl_2$-induced neurotoxicity with Doxorubicin resulted in non-significant decreased MBP level in cerebral cortices homogenates of rats of $CdCl_2$-exposure + Doxorubicin post-treated Group 7 when compared with $CdCl_2$-only treated Group 2, as presented in Table 2. These observations indicate that Doxorubicin possess neuro-protective, neuro-regenerative but less re-myelination potentials when compared with MO11 and MS06.

Total Protein evaluation determines the total concentrations of sera albumin and globulin. The results of this study showed similar Total Protein levels in cerebral homogenates of rats of Normal saline-only treated Control Group 1 and Experimental Groups 2 to 4 and 7 (Table 2). These results indicate that $CdCl_2$-exposure and post-treatments with MO11, MS06 and Doxorubicin did not negatively alter Total protein concentrations of the cerebrum in rats.

Conclusions

Overall, the observations of this study imply that post-treatments of $CdCl_2$l-induced neuro-toxicity with MO11 (from *Moringa oleifera* leaves) and MS06 (from *Musa sapientum* suckers), and Doxorubicin resulted in increased Dopamine and Glutamate levels in rats. Furthermore, post-treatments of $CdCl_2$-induced neuro-toxicity with MO11 and MS06 resulted in significant decreased levels of Myelin Basic Protein (MBP) levels, while post-treatments with Doxorubicin resulted in non-significant decreased MBP levels in rats. These observations indicate that MO11 and MS06 conferred a higher degree of neuro-protection and re-myelination potentials against $CdCl_2$-induced neurotoxicity, neuro-degeneration and de-myelination, when compared with Doxorubicin. Hence, MO11 and MS06 are recommended as potential drug candidates for the treatments of neurodegenerative disorders and diseases of the central nervous system.

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REFERENCES

1. *Afifi O.K. and Embaby A.S. (2016).* Histological study on the protective role of Ascorbic acid on Cadmium induced cerebral cortical neurotoxicity in adult male albino rats. Journal of Microscopy and Ultrastructure, 4, 36-45.
2. *Akinlolu A.A., Ameen M., QuadriT., Odubela O., Omotoso G., Yahya R., Biliaminu S., Adeyanju M., Ebito G. and Otulana J. (2020a).* Extraction, isolation and evaluation of anti-toxic principles from Moringa oleifera (MOF_6) and Myristica fragrans (Trimyristin) upregulated Acetylcholinesterase concentrations in Sodium arsenite-induced neurotoxicity in rats. Journal of Phytomedicine and Therapeutics, 19(2), 503-519.
3. *Akinlolu A.A., Sulaiman F.A., Tajudeen S., Suleiman S.K., Abdulsalam A.A. and Asogwa N.T. (2020b).* Cajanus cajan drives apoptosis via activation of caspase3/p53 pathway and possesses re-myelination and anti-gliosis potentials in Ethidium Bromide-induced neurotoxicity in rats. Nigerian Journal of Scientific Research, 19(4), 286-293.
4. *Akinlolu A.A., Oyewopo A.O., Kadir R.E., Lawal A., Ademiloye J., Jubril A., Ameen M.O. and Ebito G.E. (2021).* Moringa oleifera and Musa sapientum ameliorated 7,12-Dimethylbenz[a]anthracene-induced up-regulations of Ki67 and Multidrug resistance1 genes in rats. International Journal of Health Sciences, 15(3), 26-33.
5. *Akinlolu A.A., Ameen M., Ebito G., Asogwa N., Akindele R., Fagbounka B., Akintunde T., Odunola F., Osibowale S. and Adepeju M. (2022).* MO11 and MS06 ameliorated Cadmium Chloride-induced neuroinflammation, hyperplasia and apoptosis via NF-kB/Caspase-3/p53 pathway and down-regulated sVEGFR in rats. European Journal of Anatomy, 26(5), 495-508.
6. *Ameen M. and Akinlolu A.A. (2023).* Chromatography-Spectroscopic isolated MO11 (M. oleifera) and MS06 (M. sapientum) positively immunomodulated ACE2 levels in blood, kidney and liver of rats. Malaysian Journal of Pharmaceutical Sciences, 21(1), 15–30.
7. *Andjelkovic M., Buha D.A., Antonijevic E., Antonijevic B., Stanic M., Kotur-Stevuljevic J., Spasojevic-Kalimanovska V., Jovanovic M., Boricic N., Wallace D. and Bulat Z. (2019).* Toxic effect of acute Cadmium and Lead exposure in rat blood, liver, and kidney. International Journal of Environmental Research and Public Health, 16(2), 274. https://doi.org/10.3390/ijerph16020274.
8. *Batool Z., Agha F., Tabassum S., Batool T.S., Siddiqui R.A. and Haider S. (2019).* Prevention of Cadmiuminduced neurotoxicity in rats by essential nutrients present in nuts. Acta Neurobiologiae Experimentalis, 79, 169-183.

9. *Branca J.J.V., Fiorillo C., Carrino D., Paternostro F., Taddei N., Gulisano M., Pacini A. and Becatti M. (2020).* Cadmium-induced oxidative stress: focus on the central nervous system. Antioxidants, 9, 492. doi:10.3390/antiox9060492.

10. *Chaves N., Antonio S. and Juan, C.A. (2020).* Quantification of the antioxidant activity of plant extracts: analysis of sensitivity and hierarchization based on the method used. Antioxidants, 9(1), 76. https://doi.org/10.3390/antiox9010076.

11. *Elkhadragy M.F., Al-Olayan E.M., Al-Amiery A.A.* and *Abdel-Moneim A.E. (2018).* Protective effects of *Fragaria ananassa* extract against Cadmium Chloride-induced acute renal toxicity in rats. Biological Trace Elements Research, 181, 378-387.

12. *Elisha I.L., Botha F.S., McGaw L.J. and Eloff J.N. (2017).* The antibacterial activity of extracts of nine plant species with good activity against Escherichia coli against five other bacteria and cytotoxicity of extracts. BMC Complement Alternative Medicine, 17(1), 133. doi:10.1186/s12906-017-1645-z.

13. *El-Tarras A.E., Attia H.F., Soliman M.M., El Awady M.A. and Amin A.A. (2016).* Neuroprotective effect of grape seed extract against cadmium toxicity in male albino rats. International Journal of Immunopathology and Pharmacology, 29(3), 398–407.

14. *Gupta R., Shukla R.K., Pant A.B. and Khanna V.K. (2018).* A Dopamine-dependent activity in controlling the motor functions in Cadmium-induced neurotoxicity: Neuroprotective potential of Quercetin. Parkinsonism and Related Disorders, 46(2), e39. doi:10.1016/j.parkreldis.2017.11.127.

15. *Hugo J.O., David C.G., Ernestina H.G., Gerardo B.M. (2016).* The Role of Dopamine and its dysfunction as a consequence of oxidative stress. Oxidative Medicine and Cellular Longevity, 9730467. doi: 10.1155/2016/9730467.

16. *Omotoso G.O.,* Kadir E.R., Lewu S.F., *Gbadamosi I.T., Akinlolu A.A.,* Adunmo G.O., *Kolo R.M., Lawal M.O. and Ameen M.O. (2018).* Moringa oleifera ameliorates cuprizone-induced cerebellar damage in adult female rats. Research Journal of Health Sciences, 6(1), 13-25.

17. *Pal M.M. (2021).* Glutamate: the master neurotransmitter and its implications in chronic stress and mood disorders. Frontiers of Human Neuroscience, 15. 1-4. https://www.frontiersin.org/article/10.3389/fnhum.2021.722323

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