EAS Journal of Pharmacy and Pharmacology
Abbreviated Key Title: EAS J Pharm Pharmacol
ISSN: 2663-0990 (Print) & ISSN: 2663-6719 (Online)
Published By East African Scholars Publisher, Kenya

Volume-5 | Issue-3 | May-Jun- 2023 | DOI: 10.36349/easjpp.2023.v05i03.002

OPEN ACCESS

Original Research Article

Neurotoxic Effects of Manganese Chloride on the Cerebellar Cortex of Adult Wistar Rats

Opoola S. S[1], Ajibade A. J[1*]

[1]Department of Anatomy, LAUTECH Ogbomoso, Nigeria

Article History
Received: 04.01.2023
Accepted: 09.02.2023
Published: 23.05.2023

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: Manganese is a naturally occurring element and an essential nutrient. It is an essential trace metal that is involved in bone formation, brain development and in the metabolism of carbohydrates, cholesterol and amino acids. Excessive exposure of humans to manganese can result in a neurologic and psychological disorder called Manganism. This study assesses the effect of Manganese on the cerebellar cortex of adult wistar rats. Thirty-six (36) adult wistar rats were picked at random and divided into 4 groups with 9 animals each. Group A which was the control received distilled water, group B, group C and Group D received orally 0.3 mg/kg, 0.6 mg/kg and 0.8 mg/kg body weight of Manganese Chloride respectively for 29 days. Experimental Animals were sacrificed on the 30th day by cervical dislocation. The cerebellum were collected after sacrifice, weighted and fixed in 10% formol calcium and subsequently processed for histological observation using Hematoxylin and Eosin staining principle. Part of the cerebella cortex was homogenized for MDA, NO and SDH analysis. The result shows that the mean body weights decreased significantly in the manganese- treated groups when compared to the control. The mean brain weight of the Manganese Chloride treated groups B, C and D Insignificantly Increased compared with the control. Biochemical analysis of the MDA (Lipid Peroxide), NO (Nitric Oxide) and SDH (Succinate Dehydrogenase) Increased Significantly ($P<0.05$) in the Manganese treated group compare with the control. Histological analysis showed loss and degenerated neurons particularly the Purkinje cells in the cortical layers of the Manganese treated groups compare with normal Cerebella histoarchitecture in the control. This study concluded that Wistar rats treated with Manganese Chloride demonstrated neurodegenerative changes in the cerebella cortical layers, which may adversely affect some cerebella functions in the Wistar rats investigated.

Keywords: Manganese Chloride, Cerebellum, Cortex, Purkinje cells, degeneration.

INTRODUCTION

Manganese is a naturally occurring element and an essential nutrient. It makes up about 0.10% of the earth's crust and is the 12th most abundant element and the 5th most abundant metal, but according to Vahid *et al*., (2013), "It is the second most abundant element in the cell". Manganese is an essential trace metal that is involved in bone formation, brain development and in the metabolism of carbohydrates, cholesterol and amino acids (Ajibade *et al*., 2011).

This salt is light pink in color, Odorless and has a polymeric solid structure. It has a Molecular Weight of 125.84 g/mol, Melting Point/Range of 650°C/1202°F, and Boiling Point/Range of 1190°C/2174°F (ACROS, 2015). Manganese is absorbed by Ingestion, Inhalation and Dermal permeation, and also administered in Intravenous injection (Pan Chem *et al*., 2018).

The cerebellum derives its name as a diminutive of the word "cerebrum". This is particularly explicit in German, where the cerebellum is called Kleinhirn ("small brain") - (Rodolfo and Negrello, 2015).

It arises from the rhombencephalon or hindbrain. It is an ovoid structure that resides in the

***Corresponding Author:** Ajibade A. J
Department of Anatomy, LAUTECH Ogbomoso, Nigeria

posterior cranial fossa inferior to the tentorium cerebelli (Crumbie Lorenzo, 2020).It is neuron-rich, containing 80% of the brain's neurons organized in a dense cellular layer Dididze, (2019) and is the largest motor structure in the CNS and in humans, contains more neurons than the whole of the cerebral cortex. It is separated from the cerebrum by tentorium cerebelli, a tough layer of dura matter (Venturini, 2018) and is connected to the midbrain by the Superior Cerebellar Peduncles**,** to the Pons by the Middle Cerebellar Peduncles**,** and to the Medulla by the Inferior Cerebellar Peduncles. The Peduncles are composed of large bundles of nerve fibers connecting the cerebellum to the remainder of the nervous system (Snell, 2010). It has a weight of around 150gm (Singh, 2020). It is made of two hemispheres (Right and left cerebella hemispheres) and a narrow, worm-like central body called Vermis. Vermis is divided into Superior and Inferior Vermis. Superior vermia is located at the dorsal part of Cerebellum and the Inferior vermia is located in the ventral parts of the cerebellum (Sembuligan & Prema, 2012). There are three anatomical lobes that can be distinguished in the cerebellum; the Anterior lobe, the Posterior lobe and the Flocculonodular lobe. These lobes are divided by two fissures- the Primary and Posterolateral fissures (Venturini, 2018).

Posterolateral fissure separates the median nodulus and lateral floccule on each side from the rest of the cerebellum. The Flocculonoodular lobe, behind the posterolateral fissure, consists of paired appendages called floccule located posteriorly and inferiorly and joined medially by the nodule (part of the vermis). (Mahmoud Mohammed, 2018).

Primary fissure (Fissure Prima) is situated on the superior surface and divides the corpus cerebelli into anterior and posterior (middle) lobes. (Rajani Singh, 2020).

Cerebellum develops from the wall of the metencephalon which form pons and cerebellum, and the cavity of the metencephalon forms the superior part of the fourth ventricle. The structure of the cerebellum reflects its phylogenetic (evolutionary) development: The archicerebellum (flocculonodular lobe), the oldest part phylogenetically has connections with the vestibular apparatus, especially the vestibule of the ear. The paleocerebellum (vermis and anterior lobe) of more recent development is associated with sensory data from the limbs. The neocerebellum (posterior lobe), the newest part phylogenetically, is concerned with selective control of limb movements (Moore *et al*., 2016).

The Cerebellar cortex (Cerebellar gray matter) is made up of structures arranged in three layers (Knierim James, 2020). It has an outer molecular layer, a central layer of very large neurons called Purkinje cells and an inner granule layer. The granule layer is formed by very small neurons (with diameters of only 4-5µm), which are packed together densely in contrast to the neuronal cell bodies in the molecular layer which are sparse (Mescher, 2013).

Functionally, the cerebellum is also divided into 3 parts but in different way compared with anatomical division: Cerebrocerebellum, Spinocerebellum, Vestibulocerebellum (Venturini, 2018). It coordinates voluntary movements such as posture, balance, coordination, and speech, resulting in smooth and balanced muscular activity. It contains almost half of the brain's neurons.

The Cerebellum is supply by 3 arteries, two of which arise from the basilar artery (Harish Wankhede *et al*., 2014) and one arises from each vertebral artery. The arteries are:

- Superior Cerebellar Artery,
- Anterior Inferior Cerebellar Artery
- Posterior Inferior Cerebellar Artery.

The Venous drainage of the Cerebellum is divided into two:

1. Superficial and Deep Veins (Matthieu Delion *et al*., 2017).
2. It attaches to the brainstem by three groups of nerve fibers called the Superior, Middle and Inferior Cerebellar Peduncle, through which Efferent and Afferent fibers pass to connect with the rest of the nervous system (Marine *et al*., 2020).

MATERIAL AND METHOD

Experimental Animals

Thirty-six (36) adult Wistar rats of both sexes weighing between 120 and 200g were used for this study. The rats were fed daily with normal rat chow (purchased in Ogbomosho, Oyo state, Nigeria) and distilled water was given to the rats. All the rats were routinely inspected, screened and confirmed to be healthy during the period of acclimatization in accordance with 'Guide for the care and use of Laboratory Animal' prepared and compiled by the National Academy of Science and published by the National Institute of Health (2011).

Experimental Design and Grouping

After this period of acclimatization, the rats were then separated randomly into four groups: Group A (Control) contains 9 Males, Group B contains 9 Males, Group C contains 9 Females and Group D contains 9 Females. Group A served as the control and the rats received distilled water as contained in experimental doses during the period. Groups B, C, D received oral doses 0.3ml, 0.6ml and 0.8ml of 5mg/kg body weight of $MnCl_2$ dissolved in distilled water respectively. The substance was orally administered for three weeks. The animals were restrained by lifting the

base of the tail and placed it on a solid surface with one hand and its tail was gently pulled back, the animal is then quickly and firmly picked up by the scruff of the neck with the thumb and index finger of the other hand. The neck of the animal was extended after being restrained so that a straight line was formed between the mouth and the cardiac sphincter through the esophagus orifice. The needle was passed gently through the mouth and pharynx into the esophagus and the substance was released as the animal swallow the substance.

The body weights of the rats were taken before and during the treatment in order to monitor changes in their weights.

Animal Sacrifice and Sample Collection

The animals were sacrificed on the 30th day of administration, using cervical dislocation method. The cervical regions of the Wistar rats were dislocated to elicit a fracture at the cervical region thereby rendering the animal temporarily subconscious. This method was carried out quickly so as to prevent the autolysis. The brain of each rat was carefully dissected out, weighed using sensitive balance and the cerebellum was fixed in 10% formol calcium for routine tissue processing by light microscope.

Tissue Processing

The section was produced by normal routine histological methods of Fixation, Dehydration, Impregnation, Embedding, Sectioning and Staining with H & E described by Carleton (1967).

Photomicrography

The digital micrographs of the cerebellar cortex sections were obtained to show the morphological changes that occurred in the treated groups as compared to the control group. The photomicrographs were taken at the Department of Anatomy, Ladoke Akintola University of Technology, Ogbomosho, Oyo State, using digital Am scope (MD 900) photomicroscope.

Statistical Analysis

All data were expressed as Mean ± SEM. The statistical analysis of the results obtained in the study was evaluated and tested for significance using Student's t-test. If P –value of t-test was less than 0.05 (P< 0.05), then result was significant (*). If P –value of the t-test was greater than 0.05 (P>0.05), then that means that the result is not significant.

RESULTS

Table 1: Table showing the mean ± S.E.M of the body weights of wistar rats before and during administration

PERIOD/WEEK	GROUP A	GROUP B	GROUP C	GROUP D
Week 0	132.2 ± 7.027	145.6 ± 3.768	142.2 ± 12.56	180.0 ± 5.774***
Week 1	140.9 ± 6.156	126.0 ± 4.899	124.0 ± 3.295*	119.8 ± 6.943*
Week 2	135.6 ± 10.60	119.6 ± 4.531	120.7 ± 4.462	116.3 ± 5.969
Week 3	145.0 ± 8.238	133.3 ± 5.774	136.0 ± 7.483	127.5 ± 9.955
Week 4	151.4 ± 7.889	134.6 ± 7.194	134.4 ± 6.853	144.3 ± 6.041

Significance: P < 0.05, value greater than 0.05 were considered insignificant while values less than 0.05 (P<0.05) were considered significant (*). Values were expressed as mean ± Standard error of mean.

The Body Weight of Group A wistar rats which is the control increased from 132.2 ± 7.027 at week 0 to 151.4 ± 7.889 at week 4.

The Body Weight of Group B wistar rats which received 0.3 mg/kg doses reduced from 145.6 ± 3.768 at week 0 to 134.6 ± 7.194 at week 4.

The Body Weight of Group C rats which received 0.6 mg/kg doses reduced from 142.2 ± 12.56 at week 0 to 134.4 ± 6.853 at week 4.

The Body Weight of Group D wistar rats which received 0.8 mg/kg doses reduced from 180.0 ± 5.774*** at week 0 to 144.3 ± 6.041 at week 4.

The Body Weight of Group A wistar rats which was the control increased from week 0 to week 4.

The Body Weight of Group B wistar rats which received 0.3 mg/kg doses decreased from week 0 to week 4.

The Body Weight of Group C rats which received 0.6 mg/kg doses decreased from week 0 to week 4.

The Body Weight of Group D wistar rats which receive 0.8 mg/kg doses reduce from week 0 to week 4.

Table 2: Table showing the Brain Weights of Wistar Rats

GROUP	Brain Weight (g)	Relative Brain Weight (%)
Group A (Control)	1.50 ± 0.04	1.00
Group B (0.3ml)	1.37 ± 0.09	1.02
Group C (0.6ml)	1.52 ± 0.05	1.13
Group D (0.8ml)	1.52 ± 0.04	1.05

The table above shows the Brain Weight (g) and The Relative Brain Weight (%) of Group A to D.

Group A which was the Control has an insignificant Increase in Brain Weight of 1.50 ± 0.04 and a Relative Brain Weight of 1.00%.

Group B which received 0.3 mg/kg doses has an insignificant decrease in Brain Weight of 1.37 ± 0.02 and a Relative Brain Weight of 1.02%.

Group C which received 0.6 mg/kg doses has an insignificant Increase in Brain Weight of 1.52 ± 0.02 and a Relative Brain Weight of 1.13%.

Group D which received 0.8 mg/kg doses has an insignificant increase in Brain Weight of 1.52 ± 0.04 and a Relative Brain Weight of 1.05%.

Table 3: Table Showing the Initial and Final Body Weight

Groups	Initial Weight (g)	Final Weight (g)	% Weight Gain or Loss
A	132.2 ± 7.027	151.4 ± 7.889	19.2
B	145.6 ± 3.768	134.6 ± 7.194	-11
C	142.2 ± 12.56	134.4 ± 6.853	-7.8
D	180.0 ± 5.774***	144.3 ± 6.041	-35.7

The above table shows the changes in body weights from the beginning to the end of the treatment i.e from the initial body weight to the final body weights. It shows an Increase in the Body Weight of Group A from 132.2 ± 7.027 to 151.4 ± 7.889 and it has a Weight Gain of 19.2%. Group B which received 0.3 mg/kg doses decreased from 145.6 ± 3.768 to 134.6 ± 7.194 with a Weight loss of 11%. Group C which received 0.6 mg/kg doses decreased in body weight from 142.2 ± 12.56 to 134.4 ± 6.853 with Weight loss of 7.8%. Group D which received 0.8 mg/kg doses decreased from 180.0 ± 5.774*** to 144.3 ± 6.041 with a Weight Gain of 35.7%.

Table 4: Table showing the Biochemical Analysis of the Adult Wistar Rats

GROUPS	MDA	NO	SDH
A	20.66 ± 0.10	3.97 ± 0.30	2.319 ± 0.43
B	26.43 ± 1.90**	5.586 ± 0.40**	3.116 ± 0.50
C	24.66 ± 0.92**	5.514 ± 0.46*	3.561 ± 0.30*
D	31.39 ± 1.80***	6.357 ± 0.45***	4.324 ± 0.30**

Significance: P < 0.05, values greater than 0.05 were considered insignificant while values less than 0.05 were considered significant (*). Values were expressed as mean ± Standard error of mean.

The Table above show the effect of Malondialdehyde on the group which insignificantly (P>0.05) Increased from 20.66 ± 0.10 in Group A to 26.43 ± 1.90** in Group B. It then Increased significantly (P<0.05) to 24.66 ± 0.92** in Group C and finally Increased significantly (P>0.05) to 31.39 ± 1.80*** in Group D.

Nitric Oxide had an effect by increasing it from 3.971 ± 0.30 in Group A to 5.586 ± 0.40** in Group B. It then decreased in Group C to 5.514 ± 0.46* and finally increased to 6.357 ± 0.45*** in Group D.

Succinate Dehydrogenase is an Enzyme and it affect by Increasing from Group A to Group D. Group A increased insignificantly (P>0.05) from 2.319 ± 0.43 to 3.116 ± 0.47 in Group B. Then increased insignificantly (P>0.05) in Group C from 3.561 ± 0.2903* to 4.324 ± 0.2970**in Group D.

.

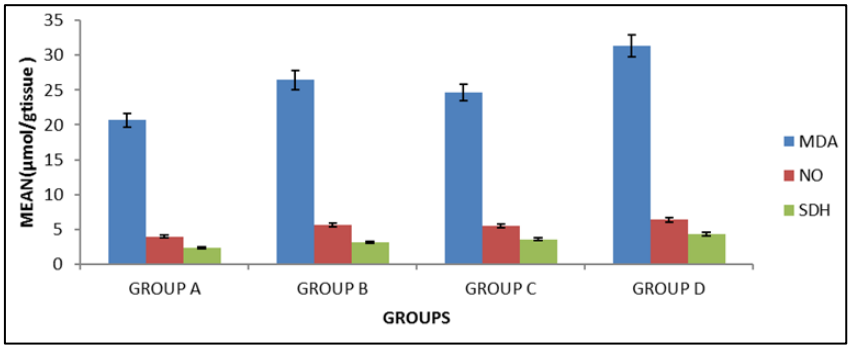

Fig. 1: Histogram showing the Biochemical Analysis of MDA, NO and SDH levels in Wistar Rats

The Chart above show the Effect of Malondialdehyde, Nitric Oxide and Succcinate Dehydrogenase on the Groups of the Adult Wistar Rats.

Effect of Malondialdehyde increased from Group A to D.

Effect on Nitric Oxide increased in Group A to D.

Effect of Succinate Dehydrogenase which is an enzyme increased from Group A which was the Control to Group D.

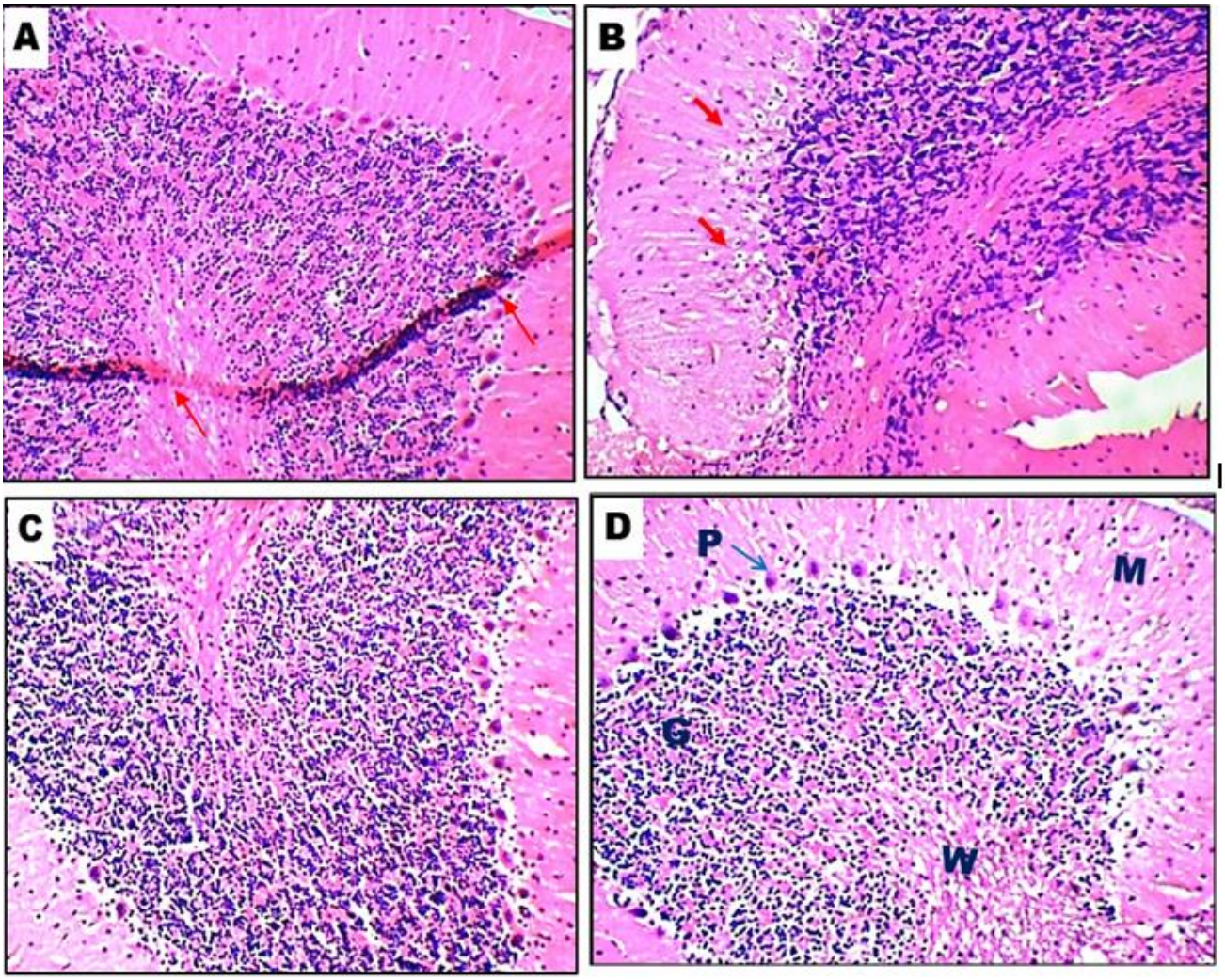

Fig. 2

X100

Fig.2 Photomicrographs of group A, B, C and D. It shows panoramic views of cerebellar cortex general morphological presentations in Wistar rats which were treated for 29 days. Group A which is the Control has a normal cerebellar cortex morphogical presentation; Group B which received 0.3 mg/kg doses has a loss and degenerating neuron in the cortical layesr. Group C which received 0.6 mg/kg doses has degenerating/pyknotic neurons and distorted neurons in the cortical layers and Group D which received 0.8 mg/kg doses has loss and degenerating/pyknotic neurons in the cortical layers (Magnification: X100).

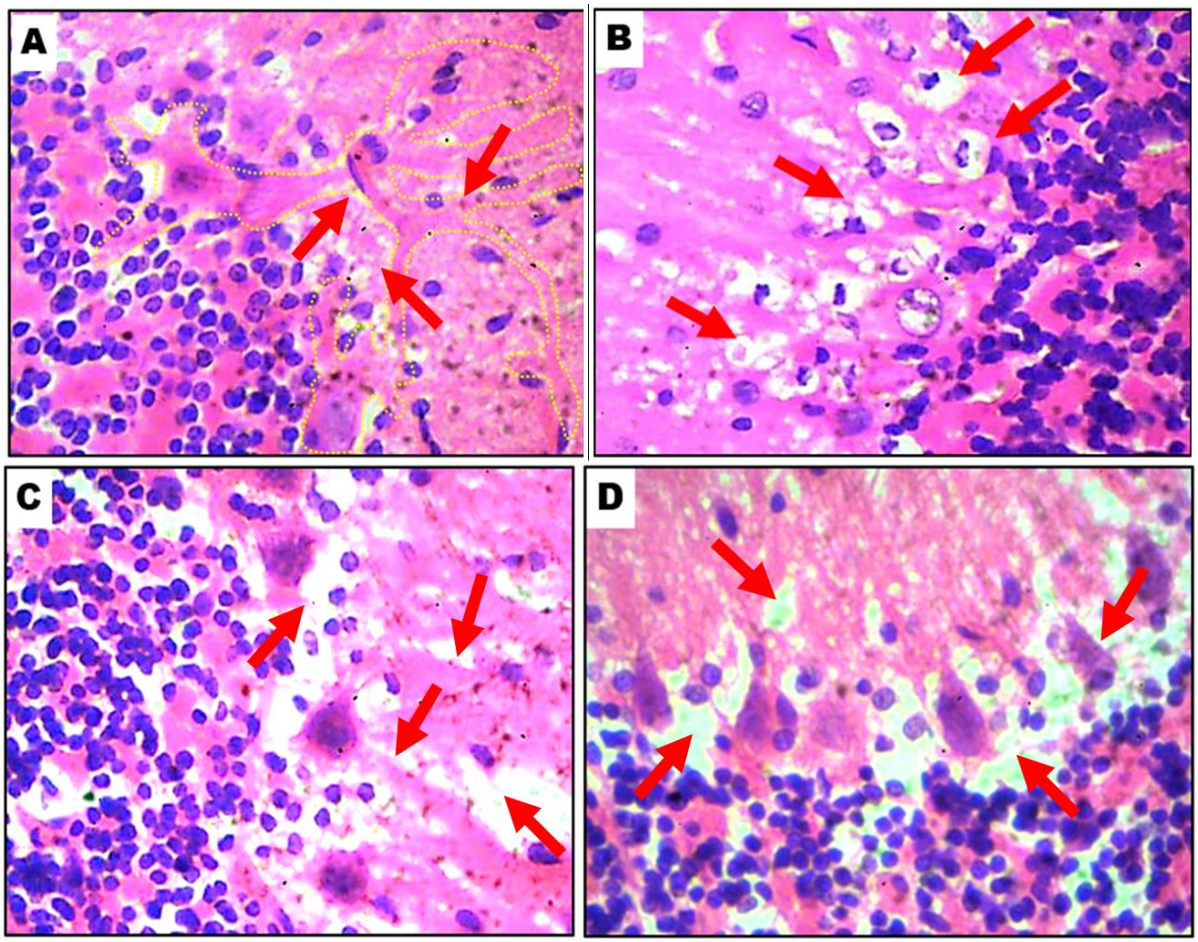

Fig. 3

X400

Fig.3 Photomicrographs of group A, B, C and D. It shows panoramic views of cerebellar cortex general morphological presentations in Wistar rats which were treated for 29 days. Group A which is the Control has a normal cerebellar cortex morphogical presentation; Group B which received 0.3 mg/kg doses has a loss and degenerating neuron in the cortical layer. Group C which received 0.6 mg/kg doses has degenerating/Pyknotic neurons and distorted neurons in the cortical layers and Group D which received 0.8 mg/kg doses has loss and degenerating/Pyknotic neurons in the cortical layers. (Magnification: X400).

RESULTS

Neither of groups A, C and D treatments altered the panoramic morphological presentation of the cortical layers from this study. In these groups, the fine arrays of cells within the cerebellar cortex can be seen distinctly arranged from the molecular to the granular layer (which surrounds the less populated medullary layer of white matter). In addition, cellular density within these groups appears normal across all cortical layers, although the Purkinje cell layers are less conspicuous at the lower magnification. The cell appears intact with distinct layering as well as intact cellular processes seen extending through the molecular layer.

Group B treatment on the other hand, induced degenerative changes in the cerebellar cortex and was characterised by fragmented granule cell layer and major parts of the neuropil appear depleted especially more conspicuous in group B treatment (red arrows). Also there appear to be a comparative reduced cell density in the cortical granular layer of these groups. Similarly, group C and D showed some degenerative changes (red arrow) with loss of cells in the cortical layers.

The transitional regions between the layers of the cerebellar cortex (Molecular (M); Purkinje (P) and Granule (G) layers) were focused at higher-power magnification to study neuronal arrangements and morphology across study groups. Normal morphological presentations of the cerebellar cortex are observable in group A. Cellular morphology in this group is characterized by Purkinje cells with conspicuous cell bodies and dendrites that are projecting deep into the molecular layers (which has sparse nuclei). Also, the granule layer in these groups consist of small granule neurons (G), which are compactly disposed in contrast to the loosely arranged and cryptic (red arrows) cells in the granule layers of

group B, C & D. Degenerating Purkinje cells (red arrow) with Pyknotic cell bodies and short dendritic processes can be seen around the indistinctly demarcated cerebellar layers of group B.

DISCUSSION

After the Experimental Study, it was discovered that Manganese II Chloride has and adverse effect on the body weight, brain weight and Increased level of Malondialdehyde (MDA), Nitric Oxide (NO), and Succinate Dehydrogenase (SDH) observed in the brain of the Adult wistar rats.

Manganese II Chloride has an adverse effect on the body weight of the Adult wistar rats by significantly decreasing the values of the weight of the body of the treated rats(Group B, C and D) in comparison to the rats in control groups(Group A). Milan and Jain, (2016) also reported that the body weight of the treated groups decreased in comparison to the control Group.

Treatment with Manganese Chloride has insignificantly increased the brain weight treated the rats (Group B, C and D) when compare to Group A which was the control. However, report from previous studies has indicated that brain weight in wistar rats treated with manganese were significantly reduced (Ajibade *et al.,* 2011). The difference in the two reports may be due to the dosage and the duration of administration.

Malondialdehyde is a highly reactive three-carbon dialdehyde produced as a byproduct of polyunsaturated fatty acid peroxidation and arachidonic acid metabolism. It is also produced in the process of prostaglandin synthesis (Marnett, 2002). MDA is also reactive species that occurs naturally and is one of a biological marker for oxidative stress, mostly existing in the enol form. MDA is produced from polyunsaturated lipids after degradation by reactive oxygen species (ROS). Among the several byproducts of Lipid Peroxidation processes, MDA is one of the most frequently used biomarkers providing an indication of the overall Lipid Peroxidation level. Lipid Peroxidation plays a role in the pathogenesis of many types of tissue injuries and especially in the tissue damage induced by several toxic substances. As one of the most known secondary products of lipid peroxidation, MDA can be used as a marker of cell membrane injury. Increased levels of lipid peroxidation products have been associated with variety of chronic diseases in human body (Jean *et al.,* 2014).

Manganese dichloride has an effect on Malondialdehyde present in the cerebellum of the brain of the wistar rat by a significant Increase in the level of the Malondialdehyde (MDA) present in the treated Group compare to the control Group. There by leading to a pathological condition. Min-Tzu chen *et al.,* (2006) reported that $MnCl_2$ increase the MDA level in the cerebellum.

Nitric oxide works as a retrograde neurotransmitter in synapses, allows the brain blood flow and also has important roles in intracellular signaling in neurons from the regulation of the neuronal metabolic status to the dendritic spine growth. Moreover, NO is able to perform post-translational modifications in proteins by the S-Nitrosylation of the thiol amino acids, which is a physiological mechanism to regulate protein function. On the other hand, during aging and pathological processes the behavior of NO can turn harmful when reacts with superoxide anion to form peroxynitrite. This gaseous compound can diffuse easily throughout the neuronal membranes damaging lipid, proteins and nucleic acids. In the case of proteins, peroxynitrite reacts mostly with the phenolic ring of the tyrosines forming nitro-tyrosines that affects dramatically to the physiological functions of the proteins. Protein nitrotyrosination is an irreversible process that also yields to the accumulation of the modified proteins contributing to the onset and progression of neurodegerative processes such as Alzhemer's disease or Parkinson's disease (Pol *et al*., 2018).

Manganese chloride affects Nitric oxide level present in the brain of the wistar rat by a significant Increase in the treated Group compare to the control Group. There by leading to a pathological condition. Chetty *et al.,* (2001) reported that $MnCl_2$ increase the NO level in the cerebellum.

The mitochondrial succinate dehydrogenase (SDH) complex catalyses the oxidation of succinate to fumarate in the krebs cycle, derived electrons being fed to the respiratory chain complex III to reduce oxygen and form water. This builds up an electrochemical gradient across the mitonchondrial inner membrane allowing for the synthesis of ATP. Alternatively, electrons can be diverted to reduce the ubiquinone pool (UQ pool) and provide reducing equivalents necessary to reduce superoxide anions originating either from an exogenous source or from the respiratory chain itself. A complete lack of succinate dehydrogenase activity will hamper electron flow to both respiratory chain complex III and the quinone pool, resulting in a major oxidative stress known to promote tumor formation in human (*Pierre et al.,* 2002). Onset of Alzheimer's, Parkinson's and Huntington's diseases as neurodegenerative disorders is increased by age. Alleviation of clinical symptoms and protection of neurons against degeneration are the main aspects of researchers to establish new therapeutic strategies. Many studies have shown that mitochondria play crucial roles in high energy demand tissues like brain.

Impairments in mitochondrial activity and physiology can makes neurons vulnerable to stress and

degeneration. Succinate dehydrogenase (SDH) connects tricarboxylic cycle to the electron transport chain. Therefore, dysfunction of the SDH could impair mitochondrial activity, ATP generation and energy hemostasis in the cell. Excess lipid synthesis, induction of the excitotoxicity in neurodegerative disorders could be controlled by SDH through direct and indirect mechanism. In addition, mutation in SDH correlates with the onset of neurodegenerative disorders. Therefore, SDH could behave as a key regulator in neuroprotection. SDH activity and related pathways are important in providing a role in neuronal survival (Mohammad *et al.*, 2018).

Manganese chloride affects Succinate dehydrogenase level present in the mitochondria of the brain of the wistar rat by a significant Increase in the treated Groups compared to the control Group. Erik *et al.*, (2017) reported that $MnCl_2$ increase the SDH level in the brain.

Histological effect of Manganese Chloride on the Cerebellum of the brain of the Adult witar rat of treated groups (B, C and D) compared to Co ntrol Group A show the degenerating/pyknotic neurons (nerve cells) in the treated groups compared to the control group. Marwa, (2019) reported on the loss or degeneration of the neuron of the cerebellum (molecular, purkinje and granular) in treated group compared to control group.

CONCLUSION

The study concluded that Manganese Chloride has degenerative effects on the neurons of the cerebellar cortex which may result in pathological condition; consequently, the cerebellar function may be adversely affected in the Wistar rats investigated.

There should be further research on the effect of Manganese II Chloride on the brain of the Wistar rats. People living in area where there is high exposure to Manganese II Chloride should reduce exposure due to Inhalation and other route of exposure.

REFERENCES

- ACROS ORGANIC. (2015). Physical and Chemical properties of Manganese II Chloride $MnCl_2$.Pg 1-7.
- Ajibade, A. J., Fakunle, P. B., Fatoba, O. O., & Olayemi, O. T. (2011). Some effects of manganese dichloride administration on the body weight, Purkinje cell population, brain, and cerebellar weights of adult Wistar rats. *J Neurosci Behav Health*, *3*(7), 87-90.
- Bonke, E., Zwicker, K., Siebels, I., & Dröse, S. (2016). Manganese Enhances Mitochondrial H_2O_2 Emission by Different Mechanisms. Clinic of Anasthesiology, Intensive-Care Medicine and Pain Therapy, University Hospital Frankfurt, Germany. *Free Radical Biology and Medicine*, *100*, S20.
- Chen, M. T., Cheng, G. W., Lin, C. C., Chen, B. H., & Huang, Y. L. (2006). Effects of acute manganese chloride exposure on lipid peroxidation and alteration of trace metals in rat brain. *Biological Trace Element Research*, *110*, 163-177.
- Chen, P., Bornhorst, J., & Aschner, M. A. (2018). Manganese metabolism in humans. *Bioscience, Landmark*, 23, 1655-1679.
- Chetty, C. S., Reddy, G. R., Suresh, A., Desaiah, D., Ali, S. F., & Slikker, W. J. (2001). Effects of Manganese on Inositol polyphosphate receptors and Nitric Oxide Synthase activity in rat brain. *Int J Toxicol*, 20, 275-280.
- Crumbie, L. (2020). Cerebellum gross anatomy: Lobes. Kenhub.
- Crumbie, L. (2020). Cerebellum gross anatomy: origin and location. Kenhub.
- Delion, M., Dinomais, M., & Mercier, P. (2017). Arteries and veins of the cerebellum. *The Cerebellum*, *16*(5-6), 880-912.
- Dzoyem, J. P., Kuete, V., & Eloff, J. N. (2014). Biochemical parameters in toxicological studies in Africa: significance, principle of methods, data interpretation, and use in plant screenings. In *Toxicological survey of African medicinal plants* (pp. 659-715). Elsevier.
- Farshbaf, M. J., & Kiani-Esfahani, A. (2018). Succinate dehydrogenase: Prospect for neurodegenerative diseases. *Mitochondrion*, *42*, 77-83.
- Jimshcleishvili, S., & Dididze, M. (2019). Neuroanatomy, Cerebellum. *Statpearls Publishing.* com
- Mahmoud, M. (2018). The Cerebellum: Anatomy of cerebellum and 4th ventricle. ANATOMY. Education. slideshare. Net.
- Marine, D. (2020). Cerebellum. *Neuroanatomy.*
- Mescher Anthony, L. (2013). Histology of Nervous System. *Junqueira's Basic Histology Text & Atlas.* 13th Edition. Pg. 175.
- Miali Chris. R/ (2016). Cerebellum: Anatomy and Function. Neuroscience in the 21st Century. Springer, New York, NY.
- Milan. C., & Jain, G. C. (2016). Manganese Chloride Induced Hepatic and Renal Toxicity in Wistar rats. *Toxicology International*, 23(3), 214.
- Moore. (2016). The Developing Human Clinical Oriented Embryology. Tenth Edition. Elsevier Inc. pg 395-396.
- Picón-Pagès, P., Garcia-Buendia, J., & Munoz, F. J. (2019). Functions and dysfunctions of nitric oxide in brain. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, *1865*(8), 1949-1967.
- Pierre, R., Arnold, M., & Agnes, R. (2002). Succinate dehydrogenase and human diseases: new

insights in to a well-known enzyme. *European Journal of Human Genetics*, 10, 189-291.

- Rajani, S. (2020). Cerebellum: Its Anatomy, Functions and Diseases. *White Matter*, 7.
- Rodolfo, & Negrello. (2015). Cerebellum. *Scholarpedia*, 10(1), 4606. Researchgate.net.
- Sembuligan, K., & Prema, (2012). Cerebellum. Sembuligan Medical Physiology textbook.
- Snell, R. S. (2010). Clinical Neuroanatomy. 7th Edition. Wolters Kluwer, *Lippincott Williams and Wilkins*, Philadelphia p. 6, 1-2.
- Vahid. (2013). Manganese. "It is the second most abundant element in the cell".
- Venturini, S. (2018). The Cerebellum: Anatomical lobes. Structures of the Central Nervous System. Neuroanatomy. *Teach Me Anatomy*, 35.
- Venturini, S. (2018). The Cerebellum: Functional Division. Structures of the Central Nervous System. Neuroanatomy. *Teach Me Anatomy*, 35.
- Wankhede, H. A., Hosmani, P. B., & Nimje, D. A. (2014). Morphological study of the basilar artery in adult human cadavers. *Int J Anat Res*, *2*(03), 497-502.

Cite This Article: Popoola S. S & Ajibade A. J (2023). Neurotoxic Effects of Manganese Chloride on the Cerebellar Cortex of Adult Wistar Rats. *EAS J Pharm Pharmacol*, *5*(3), 49-57