OPEN ACCESS
Scholars International Journal of Biochemistry
Abbreviated Key Title: Sch Int J Biochem
ISSN 2616-8650 (Print) |ISSN 2617-3476 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com/sijb

Original Research Article

Biochemical Study on Brain Oxidative Stress induced by Aluminum Chloride

Hussein A Abdel Maksoud[1], Alshaimaa M Said[1*], Mabrouk A Abdeldaiem[2], Mahmoud A Hassan[1]

[1]Biochemistry Department, Faculty of Veterinary Medicine, Benha University Menofia Governorate, Egypt
[2]Biochemistry Department, Faculty of Veterinary Medicine, Menoufia University Menofia Governorate, Egypt

DOI: 10.36348/sijb.2020.v03i10.00X | **Received:** 30.09.2020 | **Accepted:** 16.10.2020 | **Published:** X

***Corresponding author:** Alshaimaa Mohammed Said

Abstract

Neurotoxicity is a form of toxicity in which a biological, chemical, or physical agent produces an adverse effect on the structure or function of the central and/or peripheral nervous system. This study was conducted to evaluate the neurooprotective effect of aluminium chloride induced neuroyoxicity in rats. Fourty rats used in this study were divided into two groups: control group, rats were received normal laboratory diet all over the period of the experiment for 8 weeks, aluminum chloride protective group received (i.p) injection of AlCl3 daily at dose (300mg/kg).. The results revealed that injection of AlCl3 affected on oxidative stress markers. Where, levels of malondialdehyde (MDA), myeloperoxidase (MPO), total antioxidant capacity (TAC) and nitric oxide (NO) were significantly increased and AlCl3 also reduced superoxidase dismutase (SOD), glutathione peroxidase (Gpxas), catalase (CAT) and glutathione (GSH). It can be concluded that AlCl3 caused brain oxidative damage.

Key words: Aluminum chloride, Brain, Nervous system, Neurotoxicity, Oxidative stress, Rat.

Copyright © 2020 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Neurotoxicity refers to the direct or indirect effect of chemicals that disrupt the nervous system of humans or animals. Numerous chemicals can produce neurotoxic diseases in humans, and many more are used as experimental tools to disturb or damage the nervous system of animals. Some act directly on neural cells, others interfere with metabolic processes on which the nervous system is especially dependent. Some disrupt neural function, others induce maldevelopment or damage to the adult nervous system. Perturbations may appear and disappear rapidly, evolve slowly over days or weeks and regress over months or years, or cause permanent deficits. Neurotoxicity is usually self-limiting after exposure ceases and rarely progressive in the absence of continued exposure, although there may be a significant delay between exposure and manifestation of neurotoxic effects [1].

Aluminum (Al) is widely distributed in the environment representing the third prevalent element in the earth's crust [2]. The massive daily life use of Al permits easy exposure to human beings from compounds used in utensils, food additives, water purifiers and pharmaceuticals [3]. In addition, the contamination of the environment with compounds containing aluminum such as particulate matter resulting from cement factories expose the population residing near them to occupational airborne Al particulates [4]. Moreover, exploitation of bauxite mines and acid rain can cause the flux of large amounts of Al salts from insoluble minerals, increasing the risk of human contact with Al. Therefore, further research on the mechanism of Al-induced neurotoxicity is necessary to avoid the hazardous effects of Al [5].

Aluminum is categorized as a neurotoxin which has hazardous effects on the development of the brain, prenatally or postnatally, in humans and experimental animals [6]. It has been reported that the excessive Al intake for long time causes neuroinflammation and deficits in cognitive functions. Neuroinflammation alters dendritic spines density, which, in turn, influences cognitive function [7]. Aluminum can cross the blood brain barrier and accumulate in brain tissues [8] with the highest concentrations in the hippocampus [9].

MATERIAL AND METHODS

Chemicals

Aluminium Chloride was purchased from Sigma–Aldrich, St. Louis, MO, USA.

Animals

All experiments were approved by the Ethical Committee of Faculty of Veterinary Medicine, Benha University. Fourty male Wistar albino rats (150 ± 20g) were supplied by the animal house of Faculty of Veterinary Medicine, Benha University, Egypt. They were acclimatized in our animal facility for one week under controlled environmental conditions before the experiment. Fresh daily supplies of food and tape water were served ad libitum.

Experimental protocol

Rats were randomly divided into two groups (20 each) and treated for 8 consecutive weeks. Control group: normal rats received saline i.p once daily and considered as a control normal group. AlCl3 group: rats received AlCl3 (300 mg/kg, i.p.) once daily for induction Neurotoxicity [10].

Sampling

Blood samples and brain tissue specimens were collected after overnight fasting from all animal groups twice along the duration of experiment after (4 and 8 weeks).

Blood samples

Rats were fasted overnight then, blood samples collected from retro-orbital venous plexus of eyes in clean dry tubes and incubated for 30 min at room temperature to allow clotting for serum separation then centrifuged at 3000 rpm for 15 min, the clean clear serum aspirated by automatic micropipettes, received in dry sterile eppendorf tubes and kept in deep freezer (-20 °C) until used for biochemical analysis.

Tissue samples

After blood samples collected 10 rats from each group were sacrificed by decapitation, the brain was rapidly excised and clean by rinsing with ice-cold isotonic saline to remove any blood cells and clots, then put it between 2 filter papers and quickly stored in a deep freezer at temperature (-20°C) for biochemical analysis.

Preparation of brain homogenate

After two freeze-thaw cycles were performed to break the cell membranes the homogenates were centrifuged for 5 minutes at 5000 r.p.m to separate the supernatant. The supernatant was used for determination of SOD, TAC,MDA,GSH,MPO,GPxas, and CAT as an oxidative stress markers [11-14].

STATISTICAL ANALYSIS

First, all data were tested for normality and homogeneity. Then, one way analysis of variance used to determine the statistical significance of differences among groups followed by Duncan's test as post hoc for making a multiple comparisons using the Statistical Package for Social science Software (Version 25, SPSS Inc., and Chicago, IL, USA). The values were expressed as the mean ± standard error of the mean. A significant difference was used at the 0.05 probability level.

RESULTS

The obtained data demonstrated in figure (1) revealed that, administration of $AlCl_3$ to normal rats exhibited a significant decrease in CAT, SOD and GPx activities compared with control group. Moreover, administration of $AlCl_3$ to normal rats exhibited a significant increase in MPO activity when compared to control group.

The obtained data demonstrated in figure (2) revealed that, administration of $AlCl_3$ to normal rats exhibited a significant decrease in GSH concentration compared with control group. Moreover, administration of $AlCl_3$ to normal rats exhibited a significant increase in TAC and MDA concentration when compared to control group.

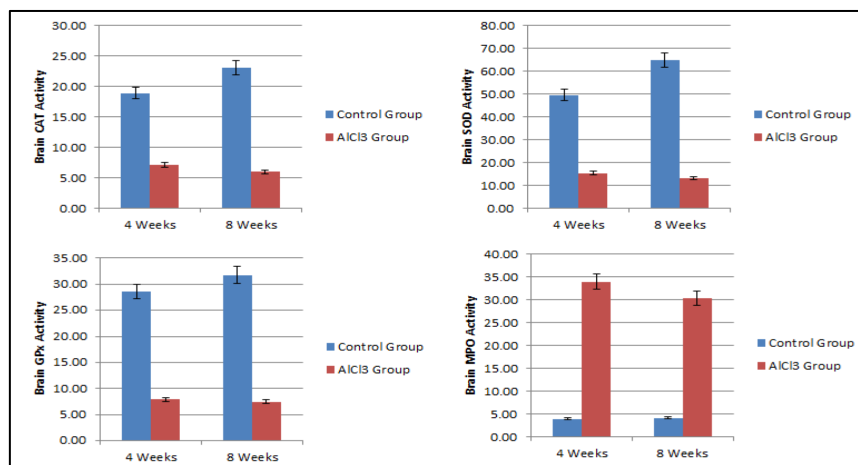

Fig-1: Effect of $AlCl_3$ on brain antioxidant enzymes

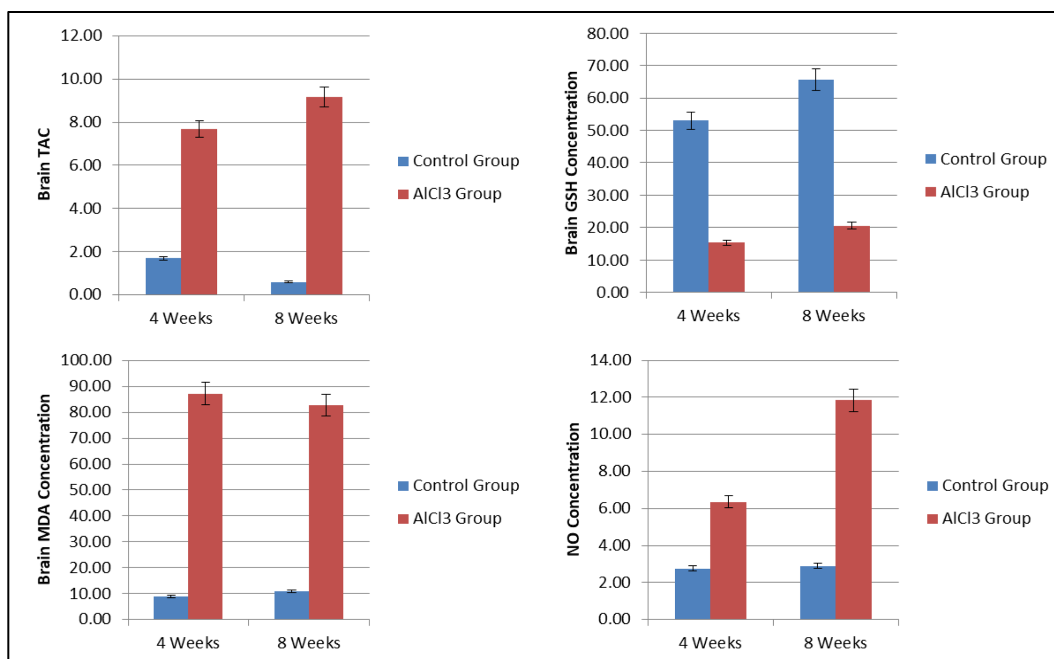

Fig-2: Effect of $AlCl_3$ on brain antioxidant enzymes

DISCUSSION

The obtained data in figures (1, 2) revealed that, injection of AlC13 to normal rats exhibited a significant increase in TAC, MDA, MPO and NO and significant decrease in SOD, GSH, GPxas and CAT when compared with control group.

These results were nearly similar to the reported studies of [15] who reported that, Brain homogenate SOD, GPxas and CAT were significantly decreased after injection of AlC13 at a dose of 34 mg/kg compared with control group. Also, [16] concluded that Brain homogenateGPxas was significantly decreased after injection of AlC13 at a dose of 50 mg/kg.

The decline in Brain homogenate SOD, GPxas and CAT after treatment with aluminium chloride (AlC13) was mainly due to the result of a reduced synthesis of the enzyme proteins as a result of higher intracellular concentrations of aluminium [17].

GSH is decreased in the brain of rats exposed to Al. In addition, [18] who reported that intrahippocampal injections of AlC13 in wistar rats induced significant increase in nitric oxide and malondialdehyde concentrations and reduced the glutathione contents at 3hrs and 30 days after treatment. Furthermore [16] reported that Chronic administration of AlC13 caused marked oxidative stress, which led to decrease in the antioxidant enzyme (SOD, CAT, and GSH) activities compared to control animals and MDA levels were found to be significantly increased compared to control animals due to an inhibition of superoxide dismutase (SOD) and catalase (CAT) activities in the brain). Thus resulting in a substantial increase in the rate of phospholipid peroxidation in brain cells, leading to membrane damage and neuron death. Also, [19] reported that a significant increase in MDA and NO level caused by AlC13 in the three studied brain regions to non-significant changes as matched with the control value and [20] reported thatAluminum-treated rats exhibited a significant decrease in CAT levels,SOD, and GPxas activities in hippocampus and cortex incomparison to controls.

Oxidative stress is defined as increased production of reactive oxygen species (ROS) that are not sufficiently removed due to impaired anti-oxidative mechanisms, which leads to progressive organ failure. Due to their high reactivity, ROS easily react with the essential molecules (proteins, lipids, DNA) and are involved in the transmission of response signal, e.g. to growth factors or cytokines [21].

Aluminiumis a ubiquitous metal and has been implicated in the etiology of Alzheimer’s disease where it exacerbates brain oxidative damage. Based on the available evidences AlC13 is considered as a putative etiological factor in a range of neurodegenerative disorders for many decades. Also, AlC13 accelerates iron mediated LPO and causes marked oxidative [22].

AlC13 accelerates iron mediated LPO and causes marked oxidative damage by increasing the redox active iron concentration in the brain. Increased oxy-radicals and loss of cellular homeostasis cause oxidative stress that lead to neurotoxicity [9]. Highly reactive and harmful chain reactions of oxygen species are generated; causing damage to living organism; reactive oxygen including superoxide free radical, hydrogen peroxide, hydroxyl free radical and singlet oxygen play a key role in the oxidative damage of different disease [23]. This in turn resulted in DNA mutation, protein inactivation, rapid peroxidation and

© 2020 |Published by Scholars Middle East Publishers, Dubai, United Arab Emirates

cell death. The oxidative damage caused by free radical is related to pathogenesis of much chronic degenerative disease like cancer, diabetes, neurodegenerative disease, atherosclerosis, cirrhosis, malaria and AIDS [24].

An imbalance in oxidant-antioxidant status is characterized by an increase in LPO and a decrease in antioxidant enzymes. Current study, AlCl3 resulted in distinct oxidative stress as indicated by increase in LPO. MDA production is assessed commonly as an indicator of LPO [25]. Earlier studies shows that increased oxidative stress upon Al induction attack almost all cell components thereby producing LPO. Studies in the past have attributed the LPO attenuating effects of fig leaves extract [26], which supports our present findings and proving its potential antioxidant ability. Taken together, our results explain that AlCl3 promotes oxidative stress by decreasing the activity of free radical-scavenging enzymes, a biological effect confirmed by increasing the levels of LPO.

CONCLUSION

The findings of this study indicate that AlCl3 one of the causes of neurotoxicity. This neurotoxicity effect of AlCl3 may be attributed to the antioxidant.

ACKNOWLEDGMENT

The authors would gratefully acknowledge the staff members in the Animal House of Biochemistry Department, Faculty of Veterinary Medicine, Benha University, Egypt for looking after the rats and for technical support in the implementation of this study.

REFERENCES

1. Spencer, P. S., & Lein, P. J. (2014). Neurotoxicity.
2. Kumar, A., Prakash, A., & Dogra, S. (2011). Neuroprotective effect of carvedilol against aluminium induced toxicity: possible behavioral and biochemical alterations in rats. Pharmacological Reports, 63(4), 915-923.
3. Bondy, S. C. (2014). Prolonged exposure to low levels of aluminum leads to changes associated with brain aging and neurodegeneration. Toxicology, 315, 1-7.
4. Boullemant, A. (2011). PM2. 5 emissions from aluminum smelters: coefficients and environmental impact. Journal of the Air & Waste Management Association, 61(3), 311-318.
5. Borgmann, U., Couillard, Y., & Grapentine, L. C. (2007). Relative contribution of food and water to 27 metals and metalloids accumulated by caged Hyalella azteca in two rivers affected by metal mining. Environmental Pollution, 145(3), 753-765.
6. Dórea, J. G. (2015). Exposure to mercury and aluminum in early life: developmental vulnerability as a modifying factor in neurologic and immunologic effects. International Journal of Environmental Research and Public Health, 12(2), 1295-1313.
7. Cao, Z., Yang, X., Zhang, H., Wang, H., Huang, W., Xu, F., ... & Li, Y. (2016). Aluminum chloride induces neuroinflammation, loss of neuronal dendritic spine and cognition impairment in developing rat. Chemosphere, 151, 289-295.
8. Li, Q., Liu, H., Alattar, M., Jiang, S., Han, J., Ma, Y., & Jiang, C. (2015). The preferential accumulation of heavy metals in different tissues following frequent respiratory exposure to PM 2.5 in rats. Scientific Reports, 5(1), 1-8.
9. Nayak, P., & Chatterjee, A. K. (2001). Effects of aluminium exposure on brain glutamate and GABA systems: an experimental study in rats. Food and chemical toxicology, 39(12), 1285-1289.
10. Amjad, S., & Umesalma, S. (2015). Protective effect of Centella asiatica against aluminium-induced neurotoxicity in cerebral cortex, striatum, hypothalamus and hippocampus of rat brain-histopathological, and biochemical approach. Journal of Molecular Biomarkers & Diagnosis, 6(1), 1.
11. Aebi, H. (1984). Catalase in vitro, Methods in enzymology, 105, 121-6.
12. Anderson, M. E. (1989). Enzymatic and chemical methods for the determination of glutathione. Glutathione: chemical, biochemical and medical aspects, 339-365.
13. Kakkar, P., Das, B., & Viswanathan, P. N. (1984). A modified spectrophotometric assay of superoxide dismutase.
14. Ohkawa, H., Ohishi, N., & Yagi, K. (1979). Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Analytical biochemistry, 95(2), 351-358.
15. Wahby, M. M., Mohammed, D. S., Newairy, A. A., Abdou, H. M., & Zaky, A. (2017). Aluminum-induced molecular neurodegeneration: The protective role of genistein and chickpea extract. Food and Chemical Toxicology, 107, 57-67.
16. Bihaqi, S. W., Sharma, M., Singh, A. P., & Tiwari, M. (2009). Neuroprotective role of Convolvulus pluricaulis on aluminium induced neurotoxicity in rat brain. Journal of ethnopharmacology, 124(3), 409-415.
17. Nehru, B., & Anand, P. (2005). Oxidative damage following chronic aluminium exposure in adult and pup rat brains. Journal of Trace Elements in Medicine and Biology, 19(2-3), 203-208.
18. Afifi, M. E. (2010). Effect of camel's milk on Cisplatin-induced nephrotoxicity in Swiss Albino mice. American journal of biochemistry and biotechnology, 6(2), 141-147.
19. Shrivastava, S. (2011). S-allyl-cysteines reduce amelioration of aluminum induced toxicity in rats. Am. J. Biochem. Biotechnol, 7(2), 74-83.
20. Elhadidy, M. E., Sawie, H. G., Meguid, N. A., & Khadrawy, Y. A. (2018). Protective effect of ashwagandha (Withania somnifera) against neurotoxicity induced by aluminum chloride in

rats. Asian Pacific Journal of Tropical Biomedicine, 8(1), 59.
21. Doungue, H. T., Kengne, A. P. N., & Kuate, D. (2018). Neuroprotective effect and antioxidant activity of Passiflora edulis fruit flavonoid fraction, aqueous extract, and juice in aluminum chloride-induced Alzheimer's disease rats. Nutrire, 43(1), 23.
22. Czechowska, G., Celinski, K., Korolczuk, A., Wojcicka, G., Dudka, J., Bojarska, A., & Reiter, R. J. (2015). Protective effects of melatonin against thioacetamide-induced liver fibrosis in rats. J Physiol Pharmacol, 66(4), 567-79.
23. Savory, J., Herman, M. M., & Ghribi, O. (2006). Mechanisms of aluminum-induced neurodegeneration in animals: Implications for Alzheimer's disease 1. Journal of Alzheimer's Disease, 10(2-3), 135-144.
24. Vertuani, S., Angusti, A., & Manfredini, S. (2004). The antioxidants and pro-antioxidants network: an overview. Current pharmaceutical design, 10(14), 1677-1694.
25. Reznick, A. Z., Shehadeh, N., Shafir, Y., & Nagler, R. M. (2006). Free radicals related effects and antioxidants in saliva and serum of adolescents with Type 1 diabetes mellitus. Archives of oral biology, 51(8), 640-648.
26. Prakash, A., Shur, B., & Kumar, A. (2013). Naringin protects memory impairment and mitochondrial oxidative damage against aluminum-induced neurotoxicity in rats. International Journal of Neuroscience, 123(9), 636-645.

© 2020 | Published by Scholars Middle East Publishers, Dubai, United Arab Emirates